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ARTICLE

Breastfeeding at night is rarely followed by hypoglycaemia in women with type 1 diabetes using carbohydrate counting and flexible insulin therapy

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Abstract

Aims/hypothesis Hypoglycaemia in association with breastfeeding is a feared condition in mothers with type 1 diabetes. Thus, routine carbohydrate intake at each breastfeed, particularly at night, is often recommended despite lack of evidence. We aimed to evaluate glucose levels during breastfeeding, focusing on whether night-time breastfeeding induced hypoglycaemia in mothers with type 1 diabetes.

Methods Of 43 consecutive mothers with type 1 diabetes, 33 (77%) were included prospectively 1 month after a singleton delivery. Twenty-six mothers (mean [SD] age 30.7 [5.8] years, mean [SD] duration of diabetes 18.6 [10.3] years) were breastfeeding and seven mothers (mean [SD] age 31.7 [5.6] years, mean [SD] duration of diabetes 20.4 [6.2] years) were bottle-feeding their infants with formula. All were experienced in carbohydrate counting using individually tailored insulin therapy with insulin analogues (45% on insulin pump, 55% on multiple daily injections). Thirty-two women with type 1 diabetes, matched for age ±1 year and BMI ±1 kg/m^2, who had not given birth or breastfed in the previous year, served as a control group. Blinded continuous glucose monitoring (CGM) for 6 days was applied at 1, 2 and 6 months postpartum in the breastfeeding mothers who recorded breastfeeds and carbohydrate intake at each CGM period. CGM was applied at 1 month postpartum in the formula-feeding mothers and once in the control women. The insulin dose was individually tailored after each CGM period.

Results The percentage of night-time spent with CGM <4.0 mmol/l was low (4.6%, 3.1% and 2.7% at each CGM period in the breastfeeding mothers vs 1.6% in the control women, $p = 0.77$), and the breastfeeding mothers spent a greater proportion of the night-time in the target range of 4.0–10.0 mmol/l ($p = 0.01$). Symptomatic hypoglycaemia occurred two or three times per week at 1, 2 and 6 months postpartum in both breastfeeding mothers and the control women. Severe hypoglycaemia was reported by one mother (3%) during the 6 month postpartum period and by one control woman (3%) in the previous year ($p = 0.74$). In breastfeeding mothers at 1 month, the insulin dose was 18% (−67% to +48%) lower than before pregnancy ($p = 0.04$). In total, carbohydrate was not consumed in relation to 438 recorded night-time breastfeeds, and CGM <4.0 mmol/l within 3 h occurred after 20 (4.6%) of these breastfeeds.

Conclusions/interpretation The percentage of night-time spent in hypoglycaemia was low in the breastfeeding mothers with type 1 diabetes and was similar in the control women. Breastfeeding at night-time rarely induced hypoglycaemia. The historical recommendation of routine carbohydrate intake at night-time breastfeeding may be obsolete in mothers with type 1 diabetes who have properly reduced insulin dose with sufficient carbohydrate intake.

Trial registration ClinicalTrials.gov NCT02898428

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Research in context

What is already known about this subject?

- Mothers with type 1 diabetes may be troubled with hypoglycaemia in relation to breastfeeding, particularly at night
- Consequently, they are advised to eat carbohydrate at each breastfeed
- In our referral area, mothers with type 1 diabetes count carbohydrates and use insulin analogues with flexible insulin therapy

What is the key question?

- Is carbohydrate intake necessary at each night-time breastfeed in mothers with type 1 diabetes who use flexible and individually tailored insulin therapy and consume an appropriate amount of carbohydrates?

What are the new findings?

- The percentage of time spent with continuous glucose monitoring (CGM) <4.0 mmol/l in the breastfeeding mothers was low and similar to that in control women with type 1 diabetes, who had not given birth or breastfed in the previous year
- Breastfeeding at night-time rarely induced hypoglycaemia and the incidence of severe hypoglycaemia was low
- Breastfeeding mothers spent more time with CGM-documented glucose levels in the target range of 4.0–10.0 mmol/l, both at night and over 24 h, compared with the control women

How might this impact on clinical practice in the foreseeable future?

- The recommended routine carbohydrate intake during night-time breastfeeding may be obsolete in mothers with type 1 diabetes who count carbohydrates and use flexible and individually tailored insulin therapy

Keywords Breastfeeding · Carbohydrate counting · Continuous glucose monitoring · Gestational weight gain retention · Hypoglycaemia · Insulin dose · Insulin pump therapy · Type 1 diabetes

Abbreviations

CGM	Continuous glucose monitoring
IOM	Institute of Medicine
SMPG	Self-monitoring of plasma glucose

Introduction

The World Health Organization recommends exclusive breastfeeding up to 6 months of age [1] to reduce the offspring's risk of future obesity [2–5], type 1 diabetes [6–8] and type 2 diabetes [9, 10]. In breastfeeding mothers with normal glucose tolerance, suckling does not affect glucose levels as documented by continuous glucose monitoring (CGM) [11, 12]. Historically, concerns that mothers with type 1 diabetes may experience hypoglycaemia soon after they breastfeed [13, 14] led to them being advised to eat before or during each breastfeeding [15]. Reducing the insulin dose by up to 27% compared with the pre-pregnancy dose has been suggested to prevent hypoglycaemia during breastfeeding [16, 17]. In 12 breastfeeding mothers with type 1 diabetes treated via insulin pump, basal insulin doses were lower during the 2 month period postpartum while the risk of hypoglycaemia was high during the first 2 weeks postpartum, although carbohydrate intake was not recorded [18].

Recently, a study of blinded CGM (i.e. the study participants could not see the measurements) applied for 6 days during breastfeeding in eight mothers with type 1 diabetes showed that the mothers spent 38% of CGM at night in hypoglycaemia (glucose levels <4.0 mmol/l) but only 9% of total CGM time in hypoglycaemia. The insulin dose during breastfeeding was at the same level as before pregnancy [19].

In the greater Copenhagen area, women with type 1 diabetes are trained to use carbohydrate counting and flexible insulin treatment with insulin analogues in either insulin pumps or basal bolus therapy.

At the maternity unit at Rigshospitalet, mothers with type 1 diabetes have for years been instructed routinely to consume 10–20 g of carbohydrate at night-time breastfeeds to avoid subsequent hypoglycaemia [20]. Besides the inconvenience of eating during the night, there is no solid evidence that this practice is necessary to obtain stable glucose levels without night-time hypoglycaemia among breastfeeding women with type 1 diabetes on flexible insulin therapy when an appropriate reduction of scheduled insulin dose and a sufficient daily carbohydrate intake are recommended postpartum.

We aimed to evaluate glucose levels during breastfeeding with intermittent CGM and focus on hypoglycaemia at night and whether night-time breastfeeding induced hypoglycaemia within 3 h of breastfeeding in mothers with type 1 diabetes on flexible insulin therapy.

Methods

Participants This prospective cohort study included Danish-speaking consecutive mothers with type 1 diabetes who delivered a single infant at the Department of Obstetrics, Rigshospitalet from 17 April 2016 to 22 October 2017 and who attended diabetes control at Steno Diabetes Center Copenhagen during pregnancy and within 3 months postpartum. This population was regarded as a random sample from the referral area.

To compare the levels of hypoglycaemia during CGM, 32 control women with type 1 diabetes, matched for age ±1 year and BMI ±1 kg/m^2, who in the preceding year had not given birth or breastfed, were identified from the electronic patient records at Steno Diabetes Center Copenhagen. All control women had a negative pregnancy test on the day of inclusion in the study.

Exclusion criteria were psychosocial barriers or a concurrent disease.

The study participants gave written informed consent to participate. The research protocol was approved by the Regional Committee on Biomedical Research Ethics (Protocol number H-16016397) and the Danish Data Protection Agency (Protocol number 2012-58-0004) and was carried out in accordance with the Declaration of Helsinki (2008). The study was registered with ClinicalTrials.gov (registration no. NCT02898428).

CGM Blinded CGM (iPro2 Professional CGM; Medtronic, Northridge, CA, USA) was applied for 6 days (mainly by L. Ringholm) to the mothers at 1 month (mean [SD] 36 [11] days), 2 months (68 [14] days) and 6 months (177 [13] days) postpartum and to the control women for one 6 day period. The CGM device was inserted according to the manufacturer's guidelines into the subcutaneous tissue of the abdominal skin. All women were encouraged to continue normal daily living during each CGM period without changing breastfeeding, food or exercise patterns.

Finger prick capillary blood glucose levels were measured with a Contour Next glucometer (Ascensia Diabetes Care Denmark, Copenhagen, Denmark) 1 and 3 h after insertion. All women were recommended to perform self-monitoring of plasma glucose (SMPG) at least four times daily, before main meals and before bedtime. The target SMPG range was 4.0–10.0 mmol/l.

Twelve mothers and four control women used CGM routinely. Of these, three agreed to use the Ipro CGM device for this study. Regardless of type of routine CGM device, the CGM data from the remaining 13 women were used in this study (Table 1).

Night-time was defined as 23:00 to 06:59 h and daytime was defined as 07:00 to 22:59 h.

Diabetes management All women were recommended an individualised diabetes diet based on the national Danish recommendations for individuals with diabetes. The breastfeeding mothers were recommended a minimum daily total carbohydrate intake of 210 g in accordance with the Institute of Medicine (IOM) guidelines to prevent ketonaemia (www.nap.edu/read/10490/chapter/8#293, accessed 31 July 2018). All were recommended to count carbohydrates from the main carbohydrate sources (bread, potatoes, rice, pasta, fruits, dairy products and confectionary) at all meals and snacks. The amount of carbohydrates from the remaining sources in a diabetes diet was judged to be 25 g daily, resulting in a recommended minimum daily intake of 185 g from main sources in breastfeeding mothers.

Based on the local treatment protocol, the insulin dose immediately postpartum was individually tailored by an endocrinologist and was intended to be approximately 60% of the pre-pregnancy dose. This involved appropriate changes in basal insulin, carbohydrate:insulin ratio and insulin sensitivity, resulting in approximately 40% reductions in basal, meal and correction insulin doses.

The insulin dose was adjusted after each CGM period, based on CGM data in combination with SMPG values, focusing on obtaining most time in the target range of 4.0–10.0 mmol/l while avoiding hypoglycaemia.

All women were recommended to do at least 30 min of exercise daily.

Breastfeeding, food and exercise diary During each 6 day CGM period the mothers were encouraged to fill in a food diary, which is used as part of routine care in our centre [21]. For this study, the diary was expanded to include breastfeeding and exercise. Each breastfeed was noted, with information on time of onset and whether an extra snack due to breastfeeding was consumed. The control women recorded a food and exercise diary during the 6 day CGM period. All women recorded self-estimated carbohydrate content from the main carbohydrate sources at all meals and snacks, as well as type and duration of exercise.

The quantity of self-estimated carbohydrate intake from the main carbohydrate sources was calculated. When in doubt, the registered dietitian (A. B. Roskjær) estimated the dimensions, weight and portion sizes based on validated tables (www.vitakost.dk/en/home, accessed 31 July 2018, www.food.dtu.dk/english/-/media/Institutter/Foedevareinstituttet/Publikationer/Pub-2013/Rapport_Maal-vaegt-og-portionsstoerrelser-paa-foedevarer.ashx?la=da, accessed 31 July 2018).

Evaluation of CGM data After each CGM period, each woman discussed the downloaded CGM data with an endocrinologist

Table 1 Baseline data for 33 mothers with type 1 diabetes and 32 control women with type 1 diabetes who in the previous year had not given birth and had not breastfed

Characteristic	Breastfeeding mothers	Formula-feeding mothers	All mothers	Control women	*p* value for all mothers vs control women
n	26	7	33	32	–
Age, years	30.7 (5.8)	31.7 (5.6)	30.9 (5.7)	31.3 (5.2)	0.63
Duration of diabetes, years	18.6 (10.3)	20.4 (6.2)	19.0 (9.5)	15.7 (8.0)	0.17
European ancestry, *n* (%)	25 (96)	5 (71)	30 (91)	31 (97)	0.61
BMI, kg/m^2	26.8 (4.9)[a]	27.0 (6.8)[a]	26.8 (5.3)[a]	26.0 (4.8)	0.39
Education level, *n* (%)					0.18
≤10 years	1 (4)	0	1 (3)	1 (3)	
11–14 years	5 (19)	5 (71)	10 (30)	4 (13)	
≥15 years	20 (77)	2 (29)	22 (67)	27 (84)	
No. of years spent at school	15.8 (2.6)	13.5 (2.0)	15.3 (2.6)	17.0 (2.1)	0.002
Insulin pump therapy, *n* (%)	12 (46)	3 (43)	15 (45)	17 (53)	0.54
Routine use of CGM, *n* (%)[b]	9 (35)	3 (43)	12 (36)	4 (13)	0.03

Data are *n* (%) or mean (SD)

[a] Pre-pregnancy BMI in mothers

[b] Two mothers and one control woman with routine use of Flash glucose monitoring used the Ipro CGM device for this study. Routine use of CGM in mothers: Medtronic (*n* = 9), Navigator (*n* = 2), Flash glucose monitoring (*n* = 1). Routine use of CGM in control women: Medtronic (*n* = 1), Dexcom (*n* = 1), Animas Vibe (*n* = 2)

(L. Ringholm or S. Engberg). The primary focus was glycaemic trends during night-time, with emphasis on the prevention of hypoglycaemia. Thereafter, hypoglycaemia and pre- and postprandial glucose values during daytime were evaluated, with focus on average daily total carbohydrate intake and day-to-day variation, aiming for glucose values in the target range of 4.0–10.0 mmol/l.

The following CGM data were recorded at night-time and over 24 h: mean glucose values; percentage of time spent with glucose values in the target range (4.0–10.0 mmol/l); percentage of time spent in hypoglycaemia (<4.0 mmol/l) and percentage of time spent in hyperglycaemia (>10.0 mmol/l).

Mild hypoglycaemia Mild hypoglycaemia was defined as events with symptoms familiar to the woman as hypoglycaemia and managed by her [22].

Severe hypoglycaemia Severe hypoglycaemia was defined as events requiring assistance from others to restore normal glucose levels [23]. Where severe hypoglycaemia occurred in the period from delivery until 6 months postpartum, we performed a structured interview previously used in prospective studies among pregnant [24, 25] and non-pregnant [22] women with type 1 diabetes. The interview was modified to also address breastfeeding.

If the control women reported severe hypoglycaemia in the previous year, a structured interview was performed on the day of inclusion in the study.

Hypoglycaemia awareness Self-estimated hypoglycaemia awareness was derived from the woman's answer to the question: 'How often do you recognise symptoms, when you have a hypo?' [22, 26]. Women answering 'always' were classified as having normal awareness, those answering 'usually' were classified as having impaired awareness and those answering 'occasionally' or 'never' were classified as having unawareness.

Questionnaires At 1, 2 and 6 months, the mothers filled in a questionnaire slightly modified from [27], focusing on breastfeeding and hypoglycaemia. The questions encompassed number of daily breastfeed sessions in the previous week, number of daily formula feedings in the previous week, mild hypoglycaemia in the previous week, severe hypoglycaemia since delivery, hypoglycaemia awareness status and smoking status. Sociodemographic data were collected in the questionnaire at inclusion.

The control women filled in a questionnaire on mild hypoglycaemia in the previous week, severe hypoglycaemia in the previous year, hypoglycaemia awareness status, smoking status and sociodemographic data.

Education level was classified in accordance with the International Standard Classification of Education and converted to three educational levels: ≤10 years, 11–14 years and ≥15 years of education (uis.unesco.org/sites/default/files/documents/international-standard-classification-of-education-isced-2011-en.pdf, accessed 31 July 2018).

Full or predominant breastfeeding was defined as six or more breastfeeding sessions daily [19]. Gestational weight gain was calculated as the difference between the last weight measured before delivery and the self-reported pre-pregnancy weight [28]. Gestational weight gain retention was defined as >5.0 kg compared with pre-pregnancy weight [29].

At 1 month postpartum, the mothers gave information on offspring gestational age, weight and length at delivery.

Information on admittance to a neonatal intensive care unit was taken from the records.

On the days of application of CGM, HbA_{1c} was measured by a TOSOH G8 Automated Glycohemoglobin Analyzer (Tosoh Corporation, Tokyo, Japan).

Small- and large-for-gestational-age infants were defined as offspring birthweight ≤10th or ≥90th percentile, respectively, adjusted for sex and gestational age [30].

Sample size Although breastfeeding mothers have been reported to spend 38% of night-time in hypoglycaemia [19], we conservatively assumed that in our population the time spent in night-time hypoglycaemia was lower (i.e. mean 18% [variance 9%] in breastfeeding mothers and mean 6% [variance 3%] in control women). Thus, these figures were used when calculating sample size. We assumed that 50% of all mothers breastfed at 2 months. A sample size of 15 or more breastfeeding mothers implied that the power of the test was well over 80% and would protect against departures from underlying assumptions of normality. However, deviation from assumed prevalence in outcome variables is common. Therefore, we included all consecutive mothers during a 1.5 year period aiming to include more than 15 mothers who breastfed at 2 months.

Statistical analyses Normally distributed data were reported as mean (SD), non-normally distributed data as median (range) and categorical data as *n* (%). All comparisons were with the breastfeeding mothers.

Continuous variables were compared by paired *t* test or non-parametric tests when appropriate. Categorical variables were compared by χ^2 test or Fisher's exact test, as appropriate.

Repeated measurements were analysed by a mixed model with participant identification as random effect to take intra-individual measurement correlation into account.

To compare repeated CGM data in the breastfeeding mothers with the CGM data in the control women, a mixed model was used with random effect of matched pairs (breastfeeding mothers and matched control women).

A two-sided *p* value <0.05 was regarded as statistically significant. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

In the study period, 48 mothers with type 1 diabetes delivered. Two mothers did not attend diabetes control within 3 months postpartum and three mothers were not approached for the study due to psychosocial barriers, leaving 43 mothers of which 33 (77%) agreed to participate in the study. CGM data were available in all 33 mothers at 1 month postpartum.

At 1 month, 26 of the 33 (79%) mothers were breastfeeding their infants and seven mothers were formula feeding. One mother discontinued breastfeeding at 1–2 months and another seven mothers discontinued breastfeeding at 2–6 months postpartum (Tables 2 and 3).

The 33 mothers and the 32 control women had comparable age, BMI, duration of diabetes and use of insulin pumps, while routine use of CGM was more prevalent in the mothers than in the control women (Table 1). Mean educational level was lower in breastfeeding mothers than in the control women (15.8 [2.6] vs 17.0 [2.1] years, $p = 0.03$), although similar percentages of breastfeeding mothers and control women had educational level ≥15 years (77% vs 84%, $p = 0.52$) (Table 1). HbA_{1c} levels were lower in the breastfeeding mothers than in the control women (Table 2).

Immediately postpartum, the actual recommended daily insulin dose (rapid- and long-acting insulin analogues) was 24% (−6% to −54%) lower than before pregnancy in the mothers on multiple daily injections while basal insulin dose was 29% (−19% to −39%) lower than before pregnancy in mothers on insulin pump therapy. In breastfeeding mothers the insulin dose at 1 month was 18% (−67% to +48%) lower than before pregnancy ($p = 0.04$). At 2 and 6 months postpartum, breastfeeding mothers' insulin dose was 14% (−54% to +57%) and 4% (−59% to +41%) lower than before pregnancy ($p = 0.08$ and $p = 0.90$), respectively.

The daily carbohydrate intake from the main sources was stable at 169–182 g among breastfeeding mothers from 1 month to 6 months postpartum (i.e. 11–24 g more than in the control women) (Table 2).

The percentage of night-time spent with CGM <4.0 mmol/l was low (4.6%, 3.1% and 2.7% at each CGM period in the breastfeeding mothers vs 1.6% in the control women, $p = 0.77$) (Table 4). The breastfeeding mothers spent more time in the target range 4.0–10.0 mmol/l and less time with CGM >10.0 mmol/l and had lower mean glucose levels compared with the control women (Table 4).

At 1, 2 and 6 months, the percentage of night-time that the breastfeeding mothers spent in the target range and with CGM <4.0 mmol/l remained stable ($p = 0.29$ and $p = 0.96$, respectively) (Table 4). The same was seen in the subgroup of mothers breastfeeding for at least 6 months ($p = 0.71$ and $p = 0.64$, respectively) (Table 5).

The time spent in target range and with CGM <4.0 mmol/l were comparable between breastfeeding mothers and control women using routine CGM and/or insulin pump (Table 6).

Breastfeeding, food and exercise diaries were available for 21 breastfeeding mothers who filled in the diaries at three (one to three) CGM periods. Combining breastfeeding data from all three CGM periods, a total of 471 night-time breastfeeds were recorded. CGM <4.0 mmol/l within 3 h after night-time breastfeeding occurred after 32 (6.8%) of all night-time breastfeeds in 15 mothers, of whom eight (53%) reported normal

Table 2 Clinical data for breastfeeding and formula-feeding mothers with type 1 diabetes and in control women with type 1 diabetes who in the preceding year had not given birth and had not breastfed

Variable	Breastfeeding mothers			Formula-feeding mothers	Control women
	1 month after delivery	2 months after delivery	6 months after delivery	1 month after delivery	
n	26	24	16	7	32
Full or predominant breastfeeding (≥6 per day), *n* (%)	25 (96)	20 (83)	12 (80)[a]	–	–
No. of breastfeeds at night-time	2 (1–4)	2 (0–4)	2 (0–4)	–	–
Recordings of breastfeeds at daytime	6 (0–11)	5 (0–12)	7 (0–12)	–	–
Normal hypoglycaemia awareness, *n* (%)	18 (72)[b]	17 (74)[b]	10 (71)[b]	4 (57)	24 (75)[b]
No of mild hypoglycaemia events in the previous week	3.8 (0–16)	2 (0–10)	3 (0–6)	2 (0–6)	3.3 (0–8.5)
Insulin dose, U/kg	0.45 (0.13)	0.48 (0.15)	0.49 (0.13)	0.55 (0.34)	0.56 (0.25)
HbA_{1c}, mmol/mol	47 (6)[‡]	52 (8)[†††]	55 (10)[†]	53 (6)[††]	62 (12)
HbA_{1c}, %	6.5 (2.7)[‡]	6.9 (2.9)[†††]	7.2 (3.1)[†]	7.0 (2.7)[††]	7.8 (3.2)
Gestational weight gain retention, kg	3.3 (−4.1 to 8.3)	2.1 (−4.7 to 11.4)	0.5 (−11.8 to 9.2)	3.7 (−3.0 to 8.8)	–
Gestational weight gain retention >5 kg, *n* (%)	9 (35)	5 (21)	2 (13)	2 (29)	–
Self-estimated carbohydrate intake from main sources, g	182 (39)[†]	169 (40)	178 (40)	140 (82)[c]	158 (43)
Self-estimated daily exercise (mainly walking), min	37 (0–138)	38 (0–156)	39 (18–108)	9 (0–42)	31 (0–108)
Current smoking, *n* (%)	1 (3.8)[‡‡]	2 (8.3)	1 (6.3)	2 (29)	7 (22)

Categorical data are *n* (%), normally distributed data are mean (SD) and non-normally distributed data are median (range)

Night-time is defined as 23:00 to 06:59 h. Gestational weight gain retention is defined as >5.0 kg compared with pre-pregnancy weight. Main carbohydrate sources are bread, potatoes, rice, pasta, fruits, dairy products and confectionary

[†] $p = 0.05$, breastfeeding mothers vs control women; [††] $p = 0.04$, breastfeeding mothers vs formula-feeding mothers; [†††] $p = 0.001$, breastfeeding mothers vs control women; [‡] $p < 0.0001$, breastfeeding mothers vs control women; [‡‡] $p = 0.03$, breastfeeding mothers vs formula-feeding mothers

[a] Data were available in 15 breastfeeding mothers

[b] Missing data: at 1 and 2 months, $n = 1$; at 6 months, $n = 2$; control women, $n = 1$

[c] Data were available in four formula-feeding mothers

hypoglycaemia awareness. At 1, 2 and 6 months, there were 11, 10 and 11 episodes with CGM <4.0 mmol/l, respectively.

Carbohydrates were not consumed in association with the majority (93%) of breastfeeds at night. Among 438 night-time breastfeeds without carbohydrate intake, 20 (4.6%) were followed by CGM <4.0 mmol/l within the following 3 h in 12 mothers, of whom five (42%) reported normal hypoglycaemia awareness.

A total of 1237 day-time breastfeeds were recorded. CGM <4.0 mmol/l within 3 h after daytime breastfeeding occurred after 72 (5.8%) of all daytime breastfeeds in 18 mothers of whom 11 (61%) reported normal hypoglycaemia awareness. At 1, 2 and 6 months, there were 28, 20 and 24 episodes with CGM <4.0 mmol/l, respectively.

The glucose levels at the beginning of breastfeedings or the timing of breastfeeds were not related to CGM <4.0 mmol/l within 3 h after breastfeeding during night- or daytime.

In the breastfeeding mothers, the number of weekly episodes of mild hypoglycaemia was lower at 2 months compared with 1 month, but this did not reach statistical significance ($p = 0.06$) (Table 2). The number of weekly episodes of mild hypoglycaemia and the proportions with normal hypoglycaemia awareness were similar in the breastfeeding mothers and in the control women (Table 2).

Severe hypoglycaemia was reported by one (3%) mother and one (3%) control woman ($p = 0.74$). The mother reported two episodes of severe hypoglycaemia within 2–4 weeks postpartum, during a period when she was manually expressing breast milk. The control woman reported one episode of severe hypoglycaemia within the previous year.

The majority of the breastfeeding mothers had no gestational weight gain retention from 2 months onwards (Table 2). Among the breastfeeding mothers at 2 months, gestational weight gain was 13.1 (3.6) kg in the 21 mothers without gestational weight gain retention and 19.2 (2.8) kg in the five mothers with gestational weight gain retention ($p = 0.004$).

No incidences of ketoacidosis were reported. Five mothers were on antihypertensive therapy, of which two received

Table 3 Baseline data for first diabetes control after delivery and pregnancy outcomes in 26 breastfeeding and seven formula-feeding mothers with type 1 diabetes

Variable	Breastfeeding mothers	Formula-feeding mothers	*p* value
n	26	7	–
First visit, no. of days after delivery	32.8 (7.2)	48.4 (13.0)	0.007
Age, years	30.7 (5.8)	31.7 (5.6)	0.77
Duration of diabetes, years	18.6 (10.3)	20.4 (6.2)	0.71
European ancestry, *n* (%)	25 (96)	5 (71)	0.11
Primipara, *n* (%)	16 (62)	4 (57)	0.74
BMI before pregnancy (kg/m^2)	26.8 (4.9)	27.0 (6.8)	0.70
Educational level, *n* (%)			0.03
≤10 years	1 (4)	0	
11–14 years	5 (19)	5 (71)	
≥15 years	20 (77)	2 (29)	
No. of years spent at school	15.8 (2.6)	13.5 (2.0)	0.03
Last HbA_{1c} before pregnancy, mmol/mol	53 (12)	55 (6)	0.12
Last HbA_{1c} before pregnancy, %	7.0 (3.2)	7.2 (2.7)	0.12
Last HbA_{1c} before delivery, mmol/mol	41 (5)	43 (3)	0.08
Last HbA_{1c} before delivery, %	5.9 (2.6)	6.1 (2.4)	0.08
Insulin pump therapy, *n* (%)	12 (46)	3 (43)	1.0
Routine use of CGM, *n* (%)[a]	9 (35)	3 (43)	0.69
Gestational weight gain, kg	14.3 (4.2)	15.3 (5.5)	0.78
Insulin dose before pregnancy, U/kg	0.55 (0.17)	0.68 (0.42)	0.58
Preeclampsia, *n* (%)	4 (15)	0	0.56
Gestational age at delivery, days	263 (8)	263 (7)	0.85
Caesarean section, *n* (%)	13 (50)	2 (29)	0.41
Small-for-gestational-age infant	0	0	–
Large-for-gestational-age infant, *n* (%)	7 (27)	3 (43)	0.65
Neonatal morbidity, *n* (%)[b]	7 (27)	1 (14)	0.65

Data are *n* (%) or mean (SD)

[a] Two breastfeeding mothers with routine use of CGM or Flash glucose monitoring used the Ipro CGM device for this study. Routine use of CGM in breastfeeding mothers: Medtronic, *n* = 7; Navigator, *n* = 1; Flash glucose monitoring, *n* = 1. Routine use of CGM in formula-feeding mothers: Medtronic, *n* = 2; Navigator, *n* = 1

[b] Neonatal hypoglycaemia requiring treatment, neonatal jaundice requiring phototherapy, respiratory distress requiring continuous positive airway pressure therapy, neonatal infection requiring antibiotic therapy

labetalol for 1–2 months postpartum. Excluding women who smoked did not change the results (data not shown).

Discussion

This prospective study with intermittent use of CGM postpartum demonstrated that breastfeeding mothers with type 1 diabetes spent a greater percentage of the night-time in the target range compared with control women, while the percentage of night-time spent with CGM <4.0 mmol/l was similar when comparing breastfeeding mothers with control women.

At the majority of night-time breastfeeds, carbohydrate was not consumed and still night-time breastfeeding was rarely followed by CGM <4.0 mmol/l within the next 3 h. This is in agreement with previous observations in eight mothers with type 1 diabetes where glucose remained over 4.0 mmol/l after the majority of suckling episodes [19] and in mothers with normal glucose tolerance where suckling did not affect glucose profiles whether or not the mothers were fasting [11, 12].

The insulin dose was reduced and specifically tailored in each mother upon delivery and then further tailored after each CGM period as indicated. The daily carbohydrate intake and amount of exercise in breastfeeding mothers were remarkably stable from 1 month to 6 months postpartum. The breastfeeding mothers consumed approximately 180 g of carbohydrate from the main sources, corresponding to 205 g in total, which is close to the recommended minimum daily total carbohydrate intake of 210 g in the IOM guidelines (www.nap.edu/read/10490/chapter/8#293, accessed 31 July 2018). The carbohydrate intake was 11–24 g higher in the breastfeeding mothers than in the control women. This intensive

Table 4 CGM data in breastfeeding and formula-feeding mothers with type 1 diabetes and in control women with type 1 diabetes who in the previous year had not given birth and had not breastfed

Variable	Breastfeeding mothers			Formula-feeding mothers 1 month after delivery	Control women	*p* value[a]
	1 month after delivery	2 months after delivery	6 months after delivery			
n	26	24[b]	16[c]	7	32	–
Time with CGM monitoring per night, min	2696 (464)	2530 (599)	2755 (632)	2051 (811)	2949 (460)	0.17
Mean glucose at night-time, mmol/l	8.3 (1.7)	8.6 (2.5)	7.9 (1.6)	9.4 (1.6)	9.7 (2.4)	0.01
Percentage time spent with glucose >10.0 mmol/l at night-time	24.5 (3.9–66.2)	26.0 (0–78.5)	19.8 (0–54.2)	40.7 (7.6–70.3)	37.8 (2.8–88.5)	0.14
Percentage time spent with glucose 4.0–10.0 mmol/l at night-time	66.6 (17.8)	61.1 (21.1)	70.1 (16.1)	52.0 (18.8)	53.0 (23.8)	0.01
Percentage time spent with glucose <4.0 mmol/l at night-time	4.6 (0–20.8)	3.1 (0–36.1)	2.7 (0–38.4)	8.2 (0–14.8)	1.6 (0–39.1)	0.77
Time with CGM monitoring per 24 h, min	8002 (1357)	7520 (1732)	8435 (1490)	6245 (2107)	8558 (1139)	0.21
Mean glucose over 24 h, mmol/l	8.4 (1.5)	8.7 (2.1)	8.1 (1.5)	9.7 (1.2)	9.8 (2.2)	0.005
Percentage time spent with glucose >10.0 mmol/l over 24 h	25.0 (4.1–63.0)	27.7 (1.1–73.5)	21.9 (2.8–59.4)	47.3 (27.5–61.5)	38.6 (6.6–88.4)	0.01
Percentage time spent with glucose 4.0–10.0 mmol/l over 24 h	66.0 (14.2)	63.3 (18.4)	68.3 (14.8)	50.2 (10.9)	52.2 (20.0)	0.01
Percentage time spent with glucose <4.0 mmol/l over 24 h	5.1 (0–19.8)	4.5 (0–22.8)	3.8 (0–29.9)	4.6 (0–10.0)	2.9 (0–21.5)	0.96

Normally distributed data are given as mean (SD) and non-normally distributed data are given as median (range)

Night-time was defined as 23:00 h to 06:59 h

[a] *p* values between breastfeeding mothers at 1, 2 and 6 months and control women

[b] Discontinuation of breastfeeding within 2 months after delivery ($n = 1$), CGM not available ($n = 1$)

[c] Discontinuation of breastfeeding within 6 months after delivery ($n = 8$), CGM not available ($n = 2$)

Table 5 CGM data in 16 mothers with type 1 diabetes who were breastfeeding for at least 6 months after delivery

Variable	1 month after delivery	2 months after delivery	6 months after delivery
Time with CGM monitoring per night, min	2760 (546)	2531 (585)	2755 (632)
Mean glucose at night-time, mmol/l	8.2 (1.8)	8.2 (2.2)	7.9 (1.6)
Percentage time spent with glucose >10.0 mmol/l at night-time	25.2 (3.9–66.2)	17.3 (0–75.4)	19.8 (0–54.2)
Percentage time spent with glucose 4.0–10.0 mmol/l at night-time	66.4 (19.1)	67.2 (20.5)	70.1 (16.1)
Percentage time spent with glucose <4.0 mmol/l at night-time	2.3 (0–13.6)	3.3 (0–36.1)	2.7 (0–38.4)
Time with CGM monitoring per 24 h, min	8098 (1552)	7627 (1727)	8435 (1490)
Mean glucose over 24 h, mmol/l	8.3 (1.5)	8.2 (1.8)	8.1 (1.5)
Percentage time spent with glucose >10.0 mmol/l over 24 h	27.6 (4.1–63.0)	19.5 (1.1–60.6)	21.9 (2.8–59.4)
Percentage time spent with glucose 4.0–10.0 mmol/l over 24 h	66.4 (14.3)	68.8 (16.0)	68.3 (14.8)
Percentage time spent with glucose <4.0 mmol/l over 24 h	4.2 (0–13.6)	4.5 (0–22.8)	3.8 (0–29.9)
HbA_{1c}, mmol/mol	47 (5)	51 (8)	56 (10)
HbA_{1c}, %	6.5 (2.6)	6.8 (2.9)	7.3 (3.1)
Insulin dose, U/kg	0.47 (0.14)	0.45 (0.11)	0.51 (0.11)
Self-estimated carbohydrate intake from main sources, g	180 (37)	173 (43)	178 (40)

Normally distributed data are given as mean (SD) and non-normally distributed data are given as median (range)

Night-time was defined as 23:00 h to 06:59 h. Main carbohydrate sources were bread, potatoes, rice, pasta, fruits, dairy products and confectionary

Table 6 Clinical data for the subgroup of women using routine CGM and/or insulin pump including 14 breastfeeding mothers with type 1 diabetes at 1 month after delivery and 17 control women with type 1 diabetes who in the previous year had not given birth and had not breastfed

Variable	Breastfeeding mothers	Control women	*p* value
No. of women on CGM only/insulin pump only/insulin pump and CGM	2/5/7	0/13/4	–
Age, years	32.1 (5.5)	32.4 (5.6)	0.94
Duration of diabetes, years	21.5 (8.5)	17.2 (7.7)	0.27
BMI, kg/m^2	27.9 (4.6)[a]	25.8 (4.8)	0.10
Time with CGM monitoring per night, min	2679 (625)	2961 (421)	0.30
Mean glucose at night-time, mmol/l	8.2 (1.7)	8.6 (1.7)	0.36
Percentage time spent with glucose >10.0 mmol/l at night-time	24.5 (3.9–66.2)	26.0 (2.8–64.0)	0.83
Percentage time spent with glucose 4.0–10.0 mmol/l at night-time	70.0 (17.2)	65.9 (18.4)	0.56
Percentage time spent with glucose <4.0 mmol/l at night-time	1.1 (0–13.6)	0.9 (0–21.4)	0.62
Time with CGM monitoring per 24 h, min	7937 (1894)	8638 (1000)	0.40
Mean glucose over 24 h, mmol/l	8.2 (1.6)	8.9 (1.6)	0.23
Percentage time spent with glucose >10.0 mmol/l over 24 h	25.0 (4.1–63.0)	28.0 (6.6–66.3)	0.37
Percentage time spent with glucose 4.0–10.0 mmol/l over 24 h	68.0 (12.7)	61.1 (16.8)	0.21
Percentage time spent with glucose <4.0 mmol/l over 24 h	3.8 (0–13.6)	2.7 (0–20.8)	0.62

Normally distributed data are given as mean (SD) and non-normally distributed data are given as median (range)

Night-time was defined as 23:00 h to 06:59 h

[a] Pre-pregnancy BMI in mothers

focus on appropriate insulin dose reduction during breastfeeding and sufficient carbohydrate intake probably contributed to the low percentage of time spent in hypoglycaemia.

The daily carbohydrate intake of around 180 g was lower than in another study [19] where breastfeeding mothers consumed 237 g of carbohydrate daily; this may partly be explained by the high night-time hypoglycaemia prevalence of 38%.

Immediately postpartum, the insulin dose was reduced by approximately 24% compared with the pre-pregnancy dose. At 1 month, the insulin dose in breastfeeding mothers remained 18% lower than the pre-pregnancy dose. Insulin requirements increased gradually over the following months. Lessons learnt from this study are that the endocrinologist did not reduce the insulin dose as much as the protocol recommended and the breastfeeding mothers increased their insulin dose between visits. However, the 18% reduction in insulin dose at 2 months is in accordance with our previous data [17] where the insulin dose was 21% lower at 2–4 months compared with pre-pregnancy dose in 105 breastfeeding mothers with type 1 diabetes. Based on these observations, we are changing our protocol so that the insulin dose immediately postpartum will be individually tailored to approximately 70% of the pre-pregnancy dose.

Mild hypoglycaemia occurred two or three times per week and the incidence of severe hypoglycaemia was low in breastfeeding mothers and control women, in agreement with previous findings at our centre [17]. The proportion of breastfeeding mothers with normal hypoglycaemia awareness remained stable at around 70% during the study, similar to the control women. However, only half of the mothers with CGM <4.0 mmol/l within 3 h after breastfeeding reported normal hypoglycaemia awareness.

The majority of the mothers were trained in using carbohydrate counting and flexible insulin therapy, therefore they were accustomed to assessing insulin dose at carbohydrate intake postpartum with an appropriately adjusted carbohydrate:insulin ratio. All the mothers were on insulin analogues, almost half were on insulin pump therapy and one-third used CGM routinely. This may also have contributed to the low percentage of time spent in hypoglycaemia.

Breastfeeding mothers had better glycaemic control than control women, as judged by mean glucose levels and the amount of time spent in the target range, despite higher carbohydrate intake and lower insulin dose. In particular, the 16 mothers who breastfed long-term and the women using diabetes technology tended to have slightly better CGM profiles with less hypoglycaemia, although the numbers were too small for solid conclusions.

Glycaemic control and risk of hypoglycaemia may change during the 6 months of breastfeeding. We therefore included three CGM periods in this study whereas glycaemic control in the control women was expected to be stable. The time spent in target range and in hypoglycaemia were comparable at 1, 2 and 6 months, suggesting that the physiological changes

during this span of breastfeeding were of lesser importance for glycaemic control.

At 2 months postpartum, the majority of the breastfeeding mothers were already within 5.0 kg of their pre-pregnancy weight. Exclusive breastfeeding increases energy consumption by 1300–1900 kJ/day in the first 6 months postpartum [18, 31]. Other factors contributing to achieving pre-pregnancy body weight include appropriate gestational weight gain, focus on quantity and quality of carbohydrate intake and total energy intake [32]. Sufficient reduction in insulin dose postpartum, limiting the need for carbohydrate intake to avoid hypoglycaemia, may also be important.

Low-carbohydrate diets are popular in healthy persons [33] and in individuals with type 1 diabetes. However, breastfeeding mothers with type 1 diabetes need to consume sufficient carbohydrates to secure sufficient milk production and to avoid ketonaemia and hypoglycaemia while breastfeeding [34]. A minimum daily total carbohydrate intake of 210 g has been suggested during breastfeeding (www.nap.edu/read/10490/chapter/8#293, accessed 31 July 2018). A daily intake of 180 g carbohydrate from the main sources, as in the current study, corresponds roughly to 205 g carbohydrate by adding approximately 25 g from vegetables and other minor sources [35]. We did not investigate whether ketonaemia occurred but there were no incidences of ketoacidosis. Starvation ketoacidosis has been reported in breastfeeding mothers without diabetes [33, 36, 37].

Our data suggest that tight glycaemic control can be maintained during breastfeeding and that glucose targets similar to those for non-breastfeeding women with type 1 diabetes can be recommended in breastfeeding mothers with type 1 diabetes using flexible insulin therapy with an appropriate insulin dose reduction immediately postpartum and sufficient carbohydrate intake.

Strengths of this study include the high participation rate (77% of eligible mothers with type 1 diabetes participating), similar to studies during pregnancy [25, 38] and higher than in a previous study investigating the first 4 weeks postpartum [39]. The mothers were matched for age and pre-pregnancy BMI with control women. The high attendance rate of unselected mothers with diabetes who recently gave birth suggests that these data are generalisable to breastfeeding mothers with diabetes, subject to early insulin dose reduction and appropriate carbohydrate intake. However, we cannot rule out that our study findings can be generalised to mothers who are not adherent to treatment regimen or not receptive to careful management practices.

The observed percentages of night-time spent in hypoglycaemia (4.6%, 3.1% and 2.7% at 1, 2 and 6 months postpartum, respectively) among breastfeeding mothers were close to those seen in the control women, and much lower than the 38% previously reported in a study where the recommended insulin dose postpartum was not reduced appropriately and recommendations regarding daily carbohydrate intake were not reported [19]. A limitation of our study is that a considerably higher number of women would be needed to evaluate whether the observed small difference between breastfeeding mothers and control women reflected a statistically significant difference. However, the observed percentages of night-time spent in hypoglycaemia are at a clinically acceptable low level and the observed difference between breastfeeding mothers and control women is probably not of clinical importance.

Educational level was lower both in the breastfeeding mothers and in all 33 mothers compared with control women. Smoking was not prevalent and correction for smoking did not affect results. The high prevalence of breastfeeding and thereby low number of formula-feeding mothers limited the possibility for subanalyses. A randomised study on breastfeeding would not be ethical. CGM data in the very early postpartum period, where hypoglycaemia may be prevalent [39], were not available.

In summary, the percentage of night-time spent in hypoglycaemia was low and similar in the breastfeeding mothers with type 1 diabetes and in control women. Breastfeeding at night-time rarely induced hypoglycaemia. The established recommendation of routine carbohydrate intake at night-time breastfeeding may be obsolete in mothers with type 1 diabetes who have properly reduced insulin dose and who have sufficient carbohydrate intake.

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Contribution statement All authors contributed to the conception and design of the study, acquired the data and analysed and interpreted data. LR drafted the article. ABR, SE, ALS, HUA, PD and ERM revised drafts critically for important intellectual content. All authors gave final approval of the version to be published. LR is responsible for the integrity of the work as a whole.

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