Il microinfusore in gravidanza: quando e perchè

Elisabetta Torlone

MISEM
A.O. S. MARIA DELLA MISERICORDIA
PERUGIA

QUANDO:

ABSTRACT

INTRODUCTION An adverse intrauterine environment in early pregnancy in women with type 1 diabetes is associated with several perinatal complications including spontaneous abortions, fetal congenital defects, and preeclampsia.

OBJECTIVES We compared metabolic parameters in the first trimester of pregnancy between women with type 1 diabetes treated with continuous subcutaneous insulin infusion (CSII) and those treated with multiple daily injections (MDI).

PATIENTS AND METHODS A total of 168 women in the first trimester of pregnancy (33 using CSII and 135 using MDI) were enrolled in this cross-sectional single-center study. Anthropometric parameters, fasting serum levels of hemoglobin A_{1c} (HbA_{1c}), lipid profile, and estimated glucose disposal rate (eGDR) were determined.

TABLE 1 Characteristics of patients using continuous subcutaneous insulin infusion and multiple daily injection

Characteristic	MDI n = 135	CSII n = 33	*P* value
gestational age at baseline, wk	8 (7–10)	8 (6–10)	0.3
maternal age at baseline, y	29 (26–32)	29 (24–32)	0.5
primipara	74 (54.8)	21 (63.6)	0.4
prepregnancy counseling	61 (45.2)	20 (60.6)	0.1
age at diagnosis of diabetes, y	17 ±8	15 ±7	0.1
duration of diabetes, y	11.8 ±7.2	12.8 ±6.6	0.5
duration of CSII therapy, mo	–	33 ±32 (6–96)	–
baseline BMI, kg/m²	23.3 (21.1–26.7)	22.3 (20.5–23.2)	0.01
baseline WHR	0.79 (0.76–0.85)	0.77 (0.73–0.80)	0.01
systolic blood pressure, mmHg	116 ±11	112 ±9	0.06
diastolic blood pressure, mmHg	72 ±8	68 ±6	0.02
patients with chronic hypertension	12 (8.9)	0 (0)	0.13
patients with diabetic nephropathy	6 (4.4)	2 (6.1)	0.7
patients with diabetic retinopathy	28 (20.7)	7 (21.2)	1.0
cigarette smoking	22 (16.3)	5 (15.1)	0.9
family history of type 2 diabetes	59 (43.7)	16 (48.5)	0.7
severe hypoglycemia during the previous 6 months	6 (4.4)	1 (3.03)	1.0
diabetic ketoacidosis during the previous 6 months	1 (0.74)	0 (0)	1.0

Data are presented as mean ± standard deviation, median (interquartile range), or number (percentage).

TABLE 2 Laboratory characteristics of patients using continuous subcutaneous insulin infusion and multiple daily injection

	MDI (n = 135)	CSII (n = 33)	*P* value
HbA_{1c}, %, mmol/mol	6.8 (5.9–8.0), 51 (41–64)	6.1 (5.8–7.1), 43 (40–54)	0.09
total cholesterol, mg/dl	170.6 ±28.3	164.9 ±24.3	0.3
HDL cholesterol, mg/dl	71.6 (61.7–83.4)	73.0 (60.5–84.5)	0.9
LDL cholesterol, mg/dl	81.3 (68.4–94.8)	78.5 (65.2–96.6)	0.6
triglycerides, mg/dl	61.8 (49.2–86.3)	53.1 (42.8–67.3)	0.004
urinary protein excretion/24 h, g	0.13 (0.09–0.20)	0.13 (0.08–0.19)	0.9
creatinine clearance, ml/min	126.7 (100.1–149.1)	127.0 (109.3–145.6)	0.8
total daily insulin requirement, units/kg	0.63 (0.46–0.80)	0.54 (0.44–0.63)	0.02
eGDR, mg/kg/min	10.5 (9.2–11.4)	11.3 (10.7–11.9)	0.0007

Data are presented as mean ± standard deviation or median (interquartile range).

Conversion factors to SI units are as follows: for total cholesterol, 0.0259; HDL, 0.0259; LDL, 0.0259; triglycerides, 0.0113

Abbreviations: eGDR, estimated glucose disposal rate; HbA_{1c}, hemoglobin A_{1c}, HDL, high-density lipoprotein; LDL, low-density lipoprotein, others, see **TABLE 1**

- Numerose malattie ostetriche hanno la loro origine nel primo trimestre.
- Nello studio in oggetto è stato indagato se la modalità di somministrazione della terapia insulinica prima della gravidanza si associa alle modifiche delle condizioni metaboliche nelle donne con diabete di tipo 1 valutate dalle prime settimane di gravidanza.
- Il trattamento CSII ha diversi effetti positivi, non solo in termini di riduzione dell'HbA1c, ma anche in un più ampio contesto metabolico.
- La regressione multipla ha dimostrato che l'uso di CSII prima gravidanza era associato con una minore HbA1c al concepimento con un migliore effetto sull'outcome fetale in relazione alla migliore glicemia media.
- Il miglior controllo glicemico era ottenuto senza una maggiore incidenza di ipoglicemia

QUANDO:

Prima del concepimento

PERCHE’:

- Il fabbisogno di insulina è molto variabile a partire dal primo trimestre fino al termine della gravidanza.
- Il fabbisogno di insulina basale può essere molto variabile nel corso della giornata con difficoltà nel raggiungere gli obiettivi con le insuline basali.
- E’ possibile modificare l’erogazione del bolo in relazione non solo ai pasti ma anche alla modifiche nei tempi di svuotamento gastrico.

Analysis of Continuous Glucose Monitoring in Pregnant Women With Diabetes: Distinct Temporal Patterns of Glucose Associated With Large-for-Gestational-Age Infants

Graham R. Law,[1] George T.H. Ellison,[1] Anna L. Secher,[2] Peter Damm,[2] Elisabeth R. Mathiesen,[2] Rosemary Temple,[3] Helen R. Murphy,[3] and Eleanor M. Scott[1]

DOI: 10.2337/dc15-0070

EPIDEMIOLOGY/HEA

RESULTS

A total of 54 of 117 (46%) women developed LGA. LGA was associated with lower mean glucose (7.0 vs. 7.1 mmol/L; $P < 0.01$) in trimester 1, with higher mean glucose in trimester 2 (7.0 vs. 6.7 mmol/L; $P < 0.001$) and trimester 3 (6.5 vs. 6.4 mmol/L; $P < 0.01$). FDA showed that glucose was significantly lower midmorning (0900–1100 h) and early evening (1900–2130 h) in trimester 1, significantly higher early morning (0330–0630 h) and throughout the afternoon (1130–1700 h) in trimester 2, and significantly higher during the evening (2030–2330 h) in trimester 3 in women whose infants were LGA.

CONCLUSIONS

FDA of CGM data identified specific times of day that maternal glucose excursions were associated with LGA. It highlights trimester-specific differences, allowing treatment to be targeted to gestational glucose patterns.

ORIGINAL ARTICLE

Closed-Loop Insulin Delivery during Pregnancy in Women with Type 1 Diabetes

Zoe A. Stewart, M.D., Malgorzata E. Wilinska, Ph.D., Sara Hartnell, B.Sc., Rosemary C. Temple, M.D., Gerry Rayman, M.D., Katharine P. Stanley, M.D., David Simmons, M.D., Graham R. Law, Ph.D., Eleanor M. Scott, M.D., Roman Hovorka, Ph.D., and Helen R. Murphy, M.D.

ABSTRACT

BACKGROUND

In patients with type 1 diabetes who are not pregnant, closed-loop (automated) insulin delivery can provide better glycemic control than sensor-augmented pump therapy, but data are lacking on the efficacy, safety, and feasibility of closed-loop therapy during pregnancy.

METHODS

We performed an open-label, randomized, crossover study comparing overnight closed-loop therapy with sensor-augmented pump therapy, followed by a continuation phase in which the closed-loop system was used day and night. Sixteen pregnant women with type 1 diabetes completed 4 weeks of closed-loop pump therapy (intervention) and sensor-augmented pump therapy (control) in random order. During the continuation phase, 14 of the participants used the closed-loop system day and night until delivery. The primary outcome was the percentage of time that overnight glucose levels were within the target range (63 to 140 mg per deciliter [3.5 to 7.8 mmol per liter]).

RESULTS

The percentage of time that overnight glucose levels were in the target range was higher during closed-loop therapy than during control therapy (74.7% vs. 59.5%; absolute difference, 15.2 percentage points; 95% confidence interval, 6.1 to 24.2; P=0.002). The overnight mean glucose level was lower during closed-loop therapy than during control therapy (119 vs. 133 mg per deciliter [6.6 vs. 7.4 mmol per liter], P=0.009). There were no significant differences between closed-loop and control therapy in the percentage of time in which glucose levels were below the target range (1.3% and 1.9%, respectively; P=0.28), in insulin doses, or in adverse-event rates. During the continuation phase (up to 14.6 additional weeks, including antenatal hospitalizations, labor, and delivery), glucose levels were in the target range 68.7% of the time; the mean glucose level was 126 mg per deciliter (7.0 mmol per liter). No episodes of severe hypoglycemia requiring third-party assistance occurred during either phase.

CONCLUSIONS

Overnight closed-loop therapy resulted in better glucose control than sensor-augmented pump therapy in pregnant women with type 1 diabetes. Women receiving day-and-night closed-loop therapy maintained glycemic control during a high proportion of the time in a period that encompassed antenatal hospital admission, labor, and delivery. (Funded by the National Institute for Health Research and others; Current Controlled Trials number, ISRCTN71510001.)

From the Wellcome Trust–Medical Research Council Institute of Metabolic Science, University of Cambridge (Z.A.S., M.E.W., R.H., H.R.M.), and Wolfson Diabetes and Endocrine Clinic, Cambridge University Hospitals NHS Foundation Trust (S.H., D.S., H.R.M.), Cambridge, the Elsie Bertram Diabetes Centre (R.C.T., H.R.M.) and the Department of Obstetrics and Gynaecology (K.P.S.), Norfolk and Norwich University Hospitals NHS Foundation Trust, and the Norwich Medical School, University of East Anglia (H.R.M.), Norwich, the Ipswich Diabetes Centre, Ipswich Hospital NHS Trust, Ipswich (G.R.), and the Division of Epidemiology and Biostatistics, Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, Leeds (G.R.L., E.M.S.) — all in the United Kingdom. Address reprint requests to Dr. Murphy at Norwich Medical School, University of East Anglia, Fl. 2, Bob Champion Research and Education Bldg., Norwich NR4 7UQ, United Kingdom, or at hm386@medschl.cam.ac.uk.

N Engl J Med 2016;375:644-54.
DOI: 10.1056/NEJMoa1602494

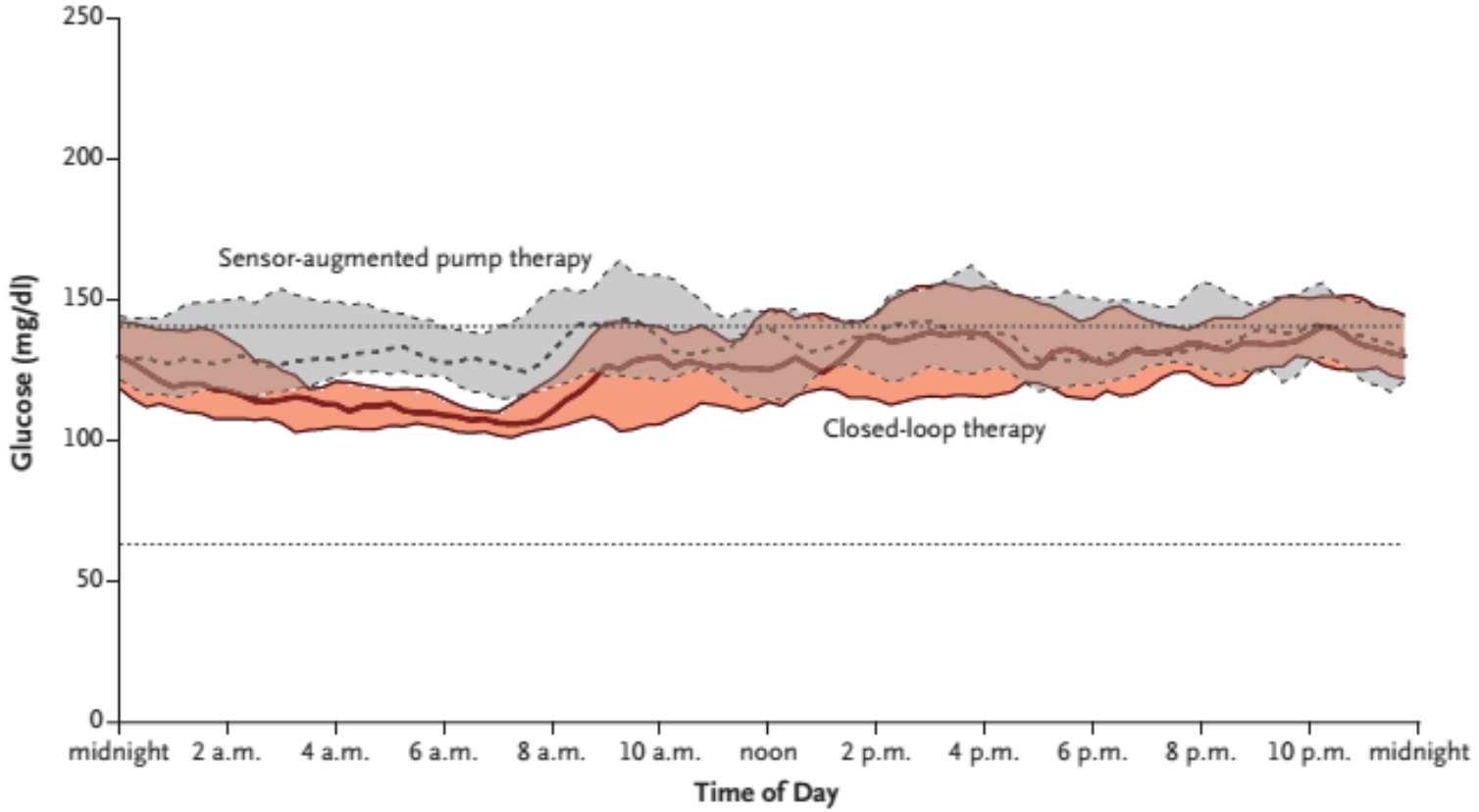

Figure 1. Median Sensor-Recorded Glucose Values over a 24-Hour Period with Sensor-Augmented Pump Therapy and Closed-Loop Insulin Delivery.

The target range for glucose values during pregnancy is 63 to 140 mg per deciliter, indicated by the two horizontal dotted lines. Functional data analysis confirmed significant differences in glucose control between the two intervention phases for a total time of 7 hours 20 minutes (from 1:50 a.m to 9:10 a.m.), with no effect of gestation and no study-phase interaction. Shading indicates the interquartile range. To convert values for glucose to millimoles per liter, multiply by 0.05551.

PERCHE’:

- La moderna terapia con CSII permette oggi e ancor più nel prossimo futuro di raggiungere obiettivi di trattamento ambiziosi e la gravidanza è sicuramente una di questi.
- La terapia con le tecnologie offre grandi opportunità ma è necessario che noi per primi siamo formati al loro uso.

Table 3. Comparison of Sensor-Augmented Pump Therapy and Closed-Loop Insulin Delivery during the Day and Evening in the Crossover Phase of the Study.*

Variable	Sensor-Augmented Pump Therapy	Closed-Loop Insulin Delivery	Absolute Difference (95% CI)	P Value
Glucose in target range (% of time)	56.8	66.3	9.4 (5.1 to 13.8)	<0.001
Glucose above target range (% of time)				
>140 mg/dl	40.9	31.6	−9.4 (−13.7 to −5.0)	<0.001
>180 mg/dl	17.3	12.6	−4.7 (−7.3 to −2.1)	0.001
Glucose below target range (% of time)				
<63 mg/dl	1.8	1.9	0.1 (−0.3 to 0.5)	0.67
<50 mg/dl	0.3	0.4	0.1 (−0.1 to 0.2)	0.52
Median no. of hypoglycemic episodes (range)	12.0 (2.0 to 26.0)	11.0 (0 to 37.0)		0.19
Mean glucose (mg/dl)	137	128	−9 (−14 to −4)	<0.001
Total insulin dose (U/day)	58.2	59.8	1.7 (−6.9 to 10.2)	0.67
Sensor wear (hr)	20.6	21.1	0.5 (−1.0 to 2.0)	0.47

* The closed-loop system was active overnight only during the crossover phase of the study, and premeal boluses were given manually (15 to 30 minutes before a meal). The reported values were derived from linear mixed-effects models.