CONTINUOUS GLUCOSE MONITORING AND PREGNANCY

Andrea Tumminia

Department of Clinical and Experimental Medicine
University of Catania
Garibaldi-Nesima Hospital
“Achieve pregnancy outcome in the diabetic woman that *approximates* that of the non-diabetic woman”
GLYCEMIC GOALS FOR PREGNANT WOMEN WITH DIABETES

Similar to the targets recommended by the American College of Obstetricians and Gynecologists (14), the ADA-recommended targets for women with type 1 or type 2 diabetes (the same as for GDM; described below) are as follows:

- Fasting \( \leq 95 \text{ mg/dL} \) (5.3 mmol/L) and either
- One-hour postprandial \( \leq 140 \text{ mg/dL} \) (7.8 mmol/L) or
- Two-hour postprandial \( \leq 120 \text{ mg/dL} \) (6.7 mmol/L)

American Diabetes Association, Standard of Medical Care in Diabetes, 2018
GLYCEMIC PROFILES DURING PREGNANCY
(women without diabetes)

Parretti E., Diabetes Care, 24:1319-23, 2001
GLUCOSE MONITORING DURING PREGNANCY

- Self Monitoring of Blood Glucose (SMBG)
- Retrospective (Blinded) Continuous Glucose Monitoring
- RT-CGM, Sensor Augmented Insulin Pump (SAP) Therapy
- The Smart Pumps (LGS, PLGS)
- Flash Glucose Monitoring (FGM)

Different study designs
Different populations
Different primary outcomes
Evolving technology
Effectiveness of continuous glucose monitoring in pregnant women with diabetes: randomised clinical trial

- **Standard antenatal care**
- **Antenatal care plus continuous glucose monitoring**

**Intervention** Continuous glucose monitoring was used as an educational tool to inform shared decision making and future therapeutic changes at intervals of 4-6 weeks during pregnancy. All other aspects of antenatal care were equal between the groups.

**Main outcome measures** The primary outcome was maternal glycaemic control during the second and third trimesters from measurements of \( \text{HbA}_{1c} \) levels every four weeks. Secondary outcomes were birth weight and risk of macrosomia using birthweight standard deviation scores and customised birthweight centiles. Statistical analyses were done on an intention to treat basis.

**Macrosomia:**
- **35% (intervention arm)**
- **60% (control arm)\ P=0.05**

*Murphy et al, BMJ 2008*
REAL-TIME (INTERMITTENT) CONTINUOUS GLUCOSE MONITORING

The Effect of Real-Time Continuous Glucose Monitoring in Pregnant Women With Diabetes

<table>
<thead>
<tr>
<th></th>
<th>Real-time CGM</th>
<th>Control subjects</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (% with type 1 diabetes)</td>
<td>79 (80)</td>
<td>75 (80)</td>
<td></td>
</tr>
<tr>
<td>Live births</td>
<td>76 (96%)</td>
<td>73 (97%)</td>
<td></td>
</tr>
<tr>
<td>Miscarriage</td>
<td>3 (4%)</td>
<td>2 (3%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Males</td>
<td>34 (45%)</td>
<td>31 (42%)</td>
<td>0.78</td>
</tr>
<tr>
<td>Weight gain in pregnancy (kg)</td>
<td>14.4 (−0.4 to 32.5)</td>
<td>13.9 (−2.0 to 31.0)</td>
<td>0.92</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>7 (9%)</td>
<td>6 (8%)</td>
<td>0.83</td>
</tr>
<tr>
<td>Caesarean section</td>
<td>28 (37%)</td>
<td>33 (45%)</td>
<td>0.30</td>
</tr>
<tr>
<td>Gestational age at birth (days)</td>
<td>263 (206–280)</td>
<td>264 (231–277)</td>
<td>0.14</td>
</tr>
<tr>
<td>Preterm delivery</td>
<td>16 (21%)</td>
<td>12 (16%)</td>
<td>0.47</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>3,510 (1,070–4,356)</td>
<td>3,436 (2,045–4,424)</td>
<td>0.80</td>
</tr>
<tr>
<td>Birth weight z-score</td>
<td>1.07 (−2.32 to 3.78)</td>
<td>0.66 (−1.13 to 3.45)</td>
<td>0.20</td>
</tr>
<tr>
<td>Large-for-gestational-age infant</td>
<td>34 (45%)</td>
<td>25 (34%)</td>
<td>0.19</td>
</tr>
<tr>
<td>2-h plasma glucose (mmol/L)</td>
<td>2.8 (0.5–5.5)</td>
<td>2.8 (1.1–6.7)</td>
<td>0.22</td>
</tr>
<tr>
<td>Neonatal hypoglycemia</td>
<td>25 (36%)</td>
<td>29 (40%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Severe neonatal hypoglycemia</td>
<td>9 (13%)</td>
<td>10 (14%)</td>
<td>0.88</td>
</tr>
<tr>
<td>Preterm delivery and/or severe neonatal hypoglycemia</td>
<td>20 (29%)</td>
<td>16 (22%)</td>
<td>0.36</td>
</tr>
</tbody>
</table>

INTERVENTION: 6 DAYS RT-CGM (8°, 12°, 21°, 27°, 33°)

COMPARABLE GLUCOSE CONTROL

COMPARABLE OUTCOMES

Secher AL et al, Diabetes Care 2013
Continuous Glucose Monitoring in Pregnancy: We Have the Technology but Not All the Answers

CGM before and during pregnancy. It is not the devices per se but how patients, their spouses/significant others, and health professionals interact with CGM that will likely determine outcomes. At this point in time we have the technology, but we don't have all the answers.

Helen R. Murphy, MBChB, FRACP, MD

Diabetes Care, volume 36, July 2013
This review found no evidence that any glucose monitoring technique is superior to any other technique among pregnant women with pre-existing type 1 or type 2 diabetes. The evidence base for the effectiveness of monitoring techniques is weak and additional evidence from large well-designed randomised trials is required to inform choices of glucose monitoring techniques.
Many studies during pregnancy, even with RT-CGM, have an average sensor use < 15 - 20% of the total time.

New England Journal of Medicine, 2010
Primary Objective: determine if RT-CGM can improve glycemic control in women with T1D who are pregnant or planning pregnancy

Results: 325 women (215 pregnant – 110 planning)

• Real-Time + SMBG vs. SMBG
• Lower HbA1c in pregnant women using CGM (mean difference −0.19%; p=0.02)
• CGM users spent more time in target (68% vs 61%; P=0.003) and less time hyperglycaemic (27% vs 32%; P=0.0279)
• Perinatal outcomes: lower incidence of: large for gestational age, neonatal intensive care admissions lasting more than 24h, neonatal hypoglycaemia. Shorter length of hospital stay

Lancet. 2017, published online September 15, 2017
Continuous Glucose Monitoring during Diabetic Pregnancy (GlucoMOMS); a multicentre randomised controlled trial

Daphne N. Voormolen PhD, J. Hans DeVries, … See all authors

First published: 30 March 2018
https://doi.org/10.1111/dom.13310

The incidence of macrosomia was 31.0% in the CGM group and 28.4% in the standard treatment group (RR 1.06, 95%CI 0.83- 1.37). HbA1c levels were similar between treatment groups.

In diabetic pregnancy, intermittent retrospective CGM use did not reduce the risk of macrosomia. CGM use provides detailed information about glycaemic fluctuations but as a treatment strategy does not translate into improved pregnancy outcome.
The detailed information provided by CGM is improving our understanding of various aspects of glucose control and in some cases deepening our understanding of the complex relationship between glucose and pregnancy outcomes.
Clinical Study
Glucose Fluctuations during Gestation: An Additional Tool for Monitoring Pregnancy Complicated by Diabetes

M. G. Dalfrà,¹ N. C. Chilelli,¹ G. Di Cianni,² G. Mello,³ C. Lencioni,² S. Biagioni,³ M. Scalese,⁴ G. Sartore,¹ and A. Lapolla¹

Women with type 1 diabetes showed a higher glycemic variability.

2-fold higher risk of hyperglycemic spikes.

HbA1c values did not correlate with glycemic variability indicators in type 1 diabetes pregnancies.
GETTING CLOSER TO THE “CLOSED LOOP”: THE SMART PUMPS

LOW GLUCOSE SUSPEND (LGS)

PREDICTIVE LOW GLUCOSE SUSPEND (PLGS)
HOW DOES IT WORK...

HYPOGLYCEMIA

BASAL INTERRUPTION
Frequency of Morning Ketosis After Overnight Insulin Suspension Using an Automated Nocturnal Predictive Low Glucose Suspend System

Diabetes Care 2014;37:1224–1229 | DOI: 10.2337/dc13-2775

The risk of development of ketosis and DKA using these systems to suspend insulin delivery is not increased.
GLUCOSE MONITORING DURING PREGNANCY

- Self Monitoring of Blood Glucose (SMBG)
- Retrospective (Blinded) Continuous Glucose Monitoring
- RT-CGM, Sensor Augmented Insulin Pump (SAP) Therapy
- The Smart Pumps (LGS, PLGS)
- Flash Glucose Monitoring (FGM)
### T1DM on MDI 17° G.W.

- PLANNED PREGNANCY (HbA1c 6.4%)
- SECOND PREGNANCY
- BREASTFEEDING OF THE FIRST BABY

### Self Monitoring of Blood Glucose

<table>
<thead>
<tr>
<th>Date</th>
<th>BB</th>
<th>AB</th>
<th>BL</th>
<th>AL</th>
<th>BD</th>
<th>AD</th>
</tr>
</thead>
<tbody>
<tr>
<td>16/02/2017</td>
<td>112</td>
<td>48</td>
<td>67</td>
<td>59</td>
<td>79</td>
<td>118</td>
</tr>
<tr>
<td>17/02/2017</td>
<td>87</td>
<td>132</td>
<td>65</td>
<td>134</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18/02/2017</td>
<td>64</td>
<td>70</td>
<td>49</td>
<td>132</td>
<td>89</td>
<td>98</td>
</tr>
<tr>
<td>19/02/2017</td>
<td>70</td>
<td>54</td>
<td>80</td>
<td></td>
<td>76</td>
<td>133</td>
</tr>
<tr>
<td>20/02/2017</td>
<td>88</td>
<td>111</td>
<td>43</td>
<td>140</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21/02/2017</td>
<td>81</td>
<td>146</td>
<td></td>
<td>68</td>
<td>109</td>
<td></td>
</tr>
<tr>
<td>22/02/2017</td>
<td>51</td>
<td>137</td>
<td>115</td>
<td>71</td>
<td>122</td>
<td></td>
</tr>
</tbody>
</table>
T1DM on MDI 21° G.W.

THREE WEEKS LATER

BREASTFEEDING

MEALS

7:30

10:00

13:00
FGM DURING PREGNANCY

Accuracy, User Acceptability, and Safety Evaluation for the FreeStyle Libre Flash Glucose Monitoring System When Used by Pregnant Women with Diabetes

Eleanor M. Scott, BM BS, MD, FRCP¹ Rudy W. Bilous, MD, FRCP² and Alexandra Kautzky-Willer, Professor, MD³

DOI 10.1186/s40220-017-0327-1

Successful glycemic control using a flash glucose monitoring system for a pregnant woman with diabetes: a case report

Miyako Kishimoto¹ ², Saori Tamada³ and Yoko Oshiba³
Efficacy of Flash Glucose Monitoring in pregnant women with poorly controlled diabetes: a randomized controlled trial

(GRUPPO DI STUDIO SID-AMD DIABETE E GRAVIDANZA)

INTERVENTION
FLASH + ≥2 SMBG per day

CONTROL
≥6 SMBG per day

45 women with pre-gest. DM (N=90)

RANDOMIZATION

45 women

PREGNANCY

7-9 months

4-8 wks

24-27 wks

36-39 wks

HbA1c
Gluc variab
Risk hypo
Risk hyper
Time in range

PREGNANCY

POST-PARTUM

1 month

4 wks post

HbA1c
Gluc variab
Risk hypo
Risk hyper
Time in range

andreatumminia@libero.it

Pregnancy outcomes

INTERVENTION
FLASH + ≥2 SMBG per day

CONTROL
≥6 SMBG per day

45 women

4-8 wks

24-27 wks

36-39 wks

HbA1c
Gluc variab
Risk hypo
Risk hyper
Time in range

INTERVENTION
FLASH + ≥2 SMBG per day

CONTROL
≥6 SMBG per day

45 women

4-8 wks

24-27 wks

36-39 wks

HbA1c
Gluc variab
Risk hypo
Risk hyper
Time in range
% of Time
(intermittent vs. continuous)

Pathophysiology insight

Smart functions LGS, PLGS

CONTINUOUS EDUCATION
Continuous Glucose Monitoring in Pregnancy: We Have the Technology but Not All the Answers

CGM before and during pregnancy. It is not the devices per se but how patients, their spouses/significant others, and health professionals interact with CGM that will likely determine outcomes. At this point in time we have the technology, but we don’t have all the answers.

Helen R. Murphy, MBCHBao, FRACP, MD

Diabetes Care, volume 36, July 2013
THANKS FOR YOUR ATTENTION