

Technology



Interpreting glycaemic patterns during pregnancy

Peter Hammond
Consultant in General Medicine, Harrogate

This commentary has often considered the role of continuous glucose monitoring (CGM) in assisting the individual with diabetes to adjust their therapy, usually insulin, but also diet, both in real-time and retrospectively in order to optimise glycaemic control. The optimal use of CGM remains controversial, but there is increasing evidence for its benefits. CGM may allow us to better understand glycaemic patterns and how we might tailor therapy for a specific population in order to achieve better population outcomes. The study by Law et al (summarised opposite) considers glycaemic profiles in pregnant women and what patterns may contribute to the development of large-for-gestational-age (LGA) babies.

The study researchers analysed CGM profiles obtained in the following two large randomised controlled trials:

1. The study from East Anglia by Murphy et al (2008), which used retrospective blinded CGM at 4 to 6 week intervals during pregnancy and showed that use of retrospective CGM led to improved control at the end of the third trimester with a lower frequency of LGA babies.
2. The study from Denmark by Secher et al (2013) of real-time CGM used for 6 days at 6-weekly intervals through pregnancy, which showed no benefit from CGM, although only 64% of women used CGM per protocol.

From both trials, 117 women had CGM profiles suitable for inclusion, and of these 89 had type 1 diabetes (76%) and 54 (46%) had LGA babies, despite near normal glycaemic control as evidenced by HbA_{1c} levels.

The women with LGA babies had significantly lower mean blood glucose values in trimester 1 compared to women who did not have LGA babies (7.0 vs 7.1 mmol/L, respectively) but had significantly higher values in the other trimesters (7.0 vs 6.7 mmol/L in trimester 2, 6.5 vs

6.4 mmol/L in trimester 3). The difference in glucose exposure was particularly notable in the second trimester with significantly greater area under the curve (AUC) for glucose >6.7 mmol/L and >7.8 mmol/L. This is consistent with previous data indicating that women with LGA babies often had better glycaemic control in early pregnancy and worse glycaemic control in later pregnancy. One hypothesis proposed to explain this observation is that women with good control in early pregnancy have better placentation, and, therefore, are better able to transfer glucose to the foetus in later pregnancy, making hyperinsulinaemia and increased foetal growth likely if blood glucose levels increase.

Where this study adds to our understanding of glucose exposure in pregnancy and the development of LGA babies is the use of functional data analysis to describe temporal patterns in glucose profiles at different stages of pregnancy. Specific time periods of lower blood glucose levels were identified in the first trimester, and higher levels were identified in the second and third trimesters, in particular 0330–0630 h and 1130–1700 h in trimester 2 and 2030–2330 h in trimester 3.

This information is valuable in highlighting where to focus efforts to lower blood glucose in women with apparently near normal glycaemic control in later pregnancy. The elevation in afternoon glucose levels in trimester 2 and evening levels in trimester 3 may reflect the slowing of post-prandial glucose disposal in later pregnancy (Murphy et al, 2012), related in part to a delay in insulin absorption and this can be mitigated by taking bolus insulin 40–60 minutes pre-prandially. The early morning elevation in the second trimester may be more difficult to address and is most amenable to change in those using insulin pump therapy. This may be a profitable target for further studies of sensor-augmented pump therapy in pregnancy. ■

Diabetes Care

Glucose variations during pregnancy

Readability /////
Applicability to practice /////
WOW! Factor /////

1 Continuous glucose monitoring (CGM) data were used to understand more fully the role that temporal glucose variation has on large-for-gestational-age (LGA) infants born to women with diabetes.

2 Data was used from two large trials of pregnant women with diabetes using CGM. In total, 117 women completing 759 measurement episodes, and providing 1.68 million glucose measurements were included in this analysis. Three-quarters of the women had T1D.

3 Just under half (46%) delivered an infant with LGA (54% delivered infants who were not LGA).

4 HbA_{1c} levels throughout pregnancy suggested that glycaemia was well controlled and there was no significant difference in HbA_{1c} between women with an LGA infant and those without.

5 LGA infants were associated with lower mean glucose (7.0 vs 7.1 mmol/L; $P<0.01$) in trimester 1, and 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; $P<0.01$) compared to no LGA.

6 Functional data analysis showed that glucose was significantly lower mid-morning and early evening in trimester 1, significantly higher early morning and throughout the afternoon in trimester 2, and significantly higher during the evening in trimester 3 in women whose infants were LGA.

7 The results from this study highlight the opportunities for more targeted treatment for pregnant women with diabetes in terms of glucose control.

Law GR, Ellison GT, Secher AL et al (2015) Analysis of continuous glucose monitoring in pregnant women with diabetes. *Diabetes Care* **38**: 1319–25

References on next page

Transpl Int

CGM use in post-operative, pancreatic transplant care

Readability ////
 Applicability to practice ///
 WOW! Factor ////

1 After receiving a pancreatic transplantation (PT) the most efficient way to measure blood glucose control appears to be continuous glucose monitoring (CGM), but at present, there is little information on the practice in this situation.

2 The study aimed to use CGM to assess the 24-hour metabolic profile of PT recipients in the early post-transplant period and to examine how these profiles relate to glucose tolerance.

3 In total, there were 30 PT recipients who were fitted with CGM systems 7 days after surgery and who completed a post-operative oral glucose tolerance test (OGTT). The CGM device was worn for 7 days or until the patient was discharged. There were 26 recipients for whom there was complete data.

4 During the monitoring phase, normoglycaemia was present 77.9% of the time. Hypoglycaemia (blood glucose <3.9 mmol/L) did occur, but times spent in hypoglycaemia were infrequent (1.4% of the time).

5 Hyperglycaemia (blood glucose >7.8 mmol/L) was more common than hypoglycaemia (20.7% of the study period time), and this correlated with the early post-operative OGTT results. Hyperglycaemia is also an indication of graft failure so it is important for clinicians to know it is happening.

6 CGM for this group of people is easy to do and provides important and useful information for clinicians.

Mittal S, Franklin RH, Policola C et al (2015) Early postoperative continuous glucose monitoring in pancreas transplant recipients. *Transpl Int* **28**: 604–9

J Diabetes Sci Technol

Hypoglycaemia prevalence in T2D

Readability ////
 Applicability to practice ////
 WOW! Factor ////

1 The prevalence of hypoglycaemia in T2D is somewhat unknown, so 108 people with T2D were fitted with a continuous glucose monitoring (CGM) system for 5 days to measure the frequency, timing and severity of hypoglycaemic events.

2 Of the cohort, nearly half had at least one hypoglycaemic episode

over the 5-day period and 75% of those individuals experienced at least one asymptomatic hypoglycaemic episode.

3 Hypoglycaemic events were most common in those that were taking insulin and oral hypoglycaemic agents (such as sulphonylureas).

4 Having the CGM system results in real-time led to treatment modifications in 64% of the participants.

5 CGM can stop hypoglycaemia and hyperglycaemia by alerting the individual to intervene and could potentially provide better overall glycaemic control.

Gehlaut RR, Dogbey GY, Schwartz FL et al (2015) Hypoglycemia in type 2 diabetes – more common than you think: a continuous glucose monitoring study. *J Diabetes Sci Technol* **27** Apr [Epub ahead of print]

Diabetes Technol Ther

Maternal glycaemia and fetal heart rate

Readability ////
 Applicability to practice ////
 WOW! Factor ///

1 Pregnant women with diabetes have increased risk of maternal and fetal adverse outcomes, which is thought to be linked to poor glycaemic control.

2 It is now possible to observe the fetal–maternal dependencies in a continuous manner using continuous glucose monitoring (CGM) on the mother and non-invasive fetal heart rate monitoring on the fetus.

3 Fourteen women who were over 30 weeks pregnant and who had T1D wore a CGM system for 48 hours but were blinded to the measurements being recorded. Records were matched with fetal electrocardiogram data collected at the same time.

4 Elevated maternal glycaemia of mothers with diabetes is significantly associated with higher odds of the fetus developing small accelerations of fetal heart rate.

Cypryk K, Bartyzel L, Zurawska-Klis M et al (2015) Continuous glucose monitoring in type 1 diabetes pregnancy shows that fetal heart rate correlates with maternal glycaemia. *Diabetes Technol Ther* **30** Apr [Epub ahead of print]

J Diabetes Res

Testing T2D resolution after LSG

Readability ///
 Applicability to practice ////
 WOW! Factor ///

1 Three years after undergoing a laparoscopic sleeve gastrectomy 20 previously morbidly obese people were deemed cured of their diabetes according to standard criteria. Researchers fitted all participants with continuous glucose monitoring (CGM) systems for 6 days to get a better understanding of their diabetes remission. Participants also completed an oral glucose tolerance test (OGTT) on day 6 of the CGM period.

2 Diabetes remission after 3 years occurred in 40% of the group. The other 60% showed a normal fasting glycaemia and HbA_{1c} but spent a substantial time in hyperglycaemia.

3 The OGTT revealed “true” T2D was present only in a small group of participants but was not specific enough to highlight those who had been in hyperglycaemia for a long period of time.

Capoccia D, Coccia F, Guida A et al (2015) Is type 2 diabetes really resolved after laparoscopic sleeve gastrectomy? Glucose variability studied by continuous glucose monitoring. *J Diabetes Res* **2015**: 674268

“Elevated maternal glycaemia of mothers with diabetes is significantly associated with higher odds of the fetus developing small accelerations of fetal heart rate.”

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Murphy HR, Rayman G, Lewis K et al (2008) Effectiveness of continuous glucose monitoring in pregnant women with diabetes: randomized controlled trial. *BMJ* **337**: a1680

Murphy HR, Eleri D, Allen JM et al (2012) Pathophysiology of postprandial hyperglycaemia in women with type 1 diabetes during pregnancy. *Diabetologia* **55**: 282–93

Secher AL, Ringholm L, Andersen HU et al (2013) The effect of real-time continuous glucose monitoring in pregnant women with diabetes: a randomized controlled trial. *Diabetes Care* **36**: 1877–83