Technology

First evidence of reduced hypoglycaemia with CGM?

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Continuous glucose monitoring (CGM) is often recommended in clinical practice to reduce the frequency of hypoglycaemia in those who are suffering significant severe hypoglycaemia or have hypoglycaemia unawareness. For example, the American Association of Clinical Endocrinologists (Harrell et al, 2010) guidelines recommend candidates include those who need to "respond to episodes of hypoglycemic unawareness and, especially, frequent or severe nocturnal hypoglycemic episodes", while the Association of British Clinical Diabetologists position statement on CGM included the indications "protection against recurrent disabling hypoglycaemia, and for those with hypoglycaemia unawareness or debilitating fear of hypoglycaemia" (Hammond et al, 2010).

Yet the evidence that CGM protects against hypoglycaemic episodes is lacking. The Juvenile Diabetes Research Foundation (JDRF) study demonstrated that in individuals with type 1 diabetes on intensified insulin therapy, CGM could improve glycaemic control when the study protocol was complied with, and CGM was used for at least 6 days per week (JDRF CGM Study Group, 2009). In those with an HbA_{1c} level <7.0% (<53 mmol/mol) at study entry, time spent in hypoglycaemia (defined by an interstitial glucose level <60 mg/dL [<3.3 mmol/L]) was significantly reduced in the CGM group compared with the control group, with a median duration of 18 versus 35 minutes per day, respectively. This, however, was not reflected by a reduction in the frequency of episodes of hypoglycaemia.

The study by Battelino et al (2011; summarised alongside) looked specifically at the potential for hypoglycaemia reduction in those using CGM with good glycaemic control, defined by an HbA_{1c} level of <7.5% (<58 mmol/mol). A total of 120 adults and children (>10 years of age) were randomised to use CGM or self-monitoring of blood glucose (SMBG) to adjust their insulin therapy. The SMBG group were also expected to wear CGM for 5 days per week to provide blinded information about time spent in the hypoglycaemic range. The CGM group were expected to set the low and high blood glucose alarms themselves but were advised of their target blood glucose range.

Some 59% of the SMBG arm and 76% of the CGM arm were using pumps. The primary outcome was time spent in hypoglycaemia and this was reduced by an average 51% in the CGM group. This effect became apparent in the first month and was sustained throughout, although the graphical representation shows an unexplained reduction in time spent in hypoglycaemia in the fifth month for the SMBG group, approaching that of the CGM group, but not evident in the sixth month. This reduction in time spent hypoglycaemic was achieved despite there also being an improvement in HbA_{1c} in the CGM group, 0.27% (3.0 mmol/mol) lower than the SMBG group at 6 months. More encouragingly, there was a trend to a reduced frequency of hypoglycaemic episodes in the CGM arm (a 30% reduction for episodes below 3.5 mmol/L; P=0.08) with a significant reduction in hypoglycaemic episodes during the night (the same reduction; P=0.009).

We therefore have the first evidence for a significant reduction in hypoglycaemic events at night. However, the individuals studied were well-motivated, testing blood glucose on average more than five times daily at study entry, and were not prone to hypoglycaemia. There were very few episodes of severe hypoglycaemia so we still lack evidence to support the recommendations included in many guidelines for CGM. This study provides limited support for a reduced frequency of hypoglycaemia associated with CGM use, but more studies are needed in the groups of hypoglycaemia sufferers for whom the technology is being promoted.

Hammond PJ, Amiel SA, Dayan CM et al (2010) ABCD position statement on continuous glucose monitoring: use of glucose sensing in outpatient clinical diabetes care. *Practical Diabetes International* **27**: 66–8

Harrell RM, Orzeck EA; American Association of Clinical Endocrinologists Socioeconomics and Member Advocacy Committee (2010) Coding guidelines for continuous glucose monitoring. *Endocr Pract* **16**: 151–4

Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group (2009) The effect of continuous glucose monitoring in well-controlled type 1 diabetes. *Diabetes Care* **32**: 1378–83

DIABETES CARE

CGM reduces hypolgycaemia and improves HbA_{1c}

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 This 26-week, randomised, controlled, multicentre study was undertaken to assess the impact of continuous glucose monitoring (CGM) on hypoglycaemia in 120 children and adults with T1D.

2 Participants on intensive therapy and an HbA_{1c} level of <7.5% (<58 mmol/mol) were randomised to either real-time CGM or conventional home monitoring with a blood glucose meter and wearing a masked continuous glucose monitor every second week for 5 days.

3 The primary outcome was time spent in hypoglycaemia (interstitial glucose concentration, <63 mg/dL [<3.5 mmol/L]).

4 Time spent in hypoglycaemia was significantly shorter in the CGM group compared with the control group: mean time, 0.48 vs 0.97 hrs/day, respectively; ratio of means, 0.49 (95% confidence interval [CI], 0.26–0.76; P=0.03).

5 At 26 weeks, HbA_{1c} levels in the CGM group were significantly lower than in the control group (difference, –0.27% [–3.0 mmol/mol]; 95% CI, –0.47 to –0.07; P=0.008).

6 Participants in the CGM group spent a significantly longer time in normoglycaemia (defined as 70–180 mg/dL [3.9–10 mmol/L]) compared with the control group (mean hours per day, 17.6 vs 16.0; P=0.009).

7 The authors concluded that, in this cohort of children and adults with T1D, CGM was associated with reduced time spent in hypoglycaemia and a concomitant decrease in HbA_{1c} levels.

Battelino T, Phillip M, Bratina N et al (2011) Effect of continuous glucose monitoring on hypoglycemia in type 1 diabetes. *Diabetes Care* **34**: 795–800

DIABETES TECHNOLOGY & THERAPEUTICS

Mean amplitude of glycaemic excursion from CGM data

Readability	✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓✓

1 The author aimed to develop an automated method to calculate mean amplitude of glycaemic excursion (MAGE) using continuous glucose monitoring (CGM) data.

2 The algorithm developed identifies the glycaemic peaks and nadirs required for MAGE calculation.

3 The algorithm generates a plot joining the peaks and nadirs required for estimating MAGE. Estimates are returned for both upward and downward excursions, along with several other indices of glycaemic variability.

4 The plots generated when applied to 104 CGM datasets, on visual inspection, were all found to have identified the peaks, nadirs and excursions correctly.

5 It was concluded that this automated algorithm eliminates the tedium and/or errors associated with manual calculation of MAGE.

Baghurst PA (2011) Calculating the mean amplitude of glycemic excursion from continuous glucose monitoring data: an automated algorithm. *Diabetes Technol Ther* **13**: 296–302

DIABETES CARE

Variability between HbA_{1c} and mean glucose levels

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 This study aimed to determine the relationship between HbA_{1c} level and mean sensor glucose concentrations in a cohort of people with T1D (n=252) from the Juvenile Diabetes Research Foundation Continuous Glucose Monitoring trial.

2 For every 1% change in HbA_{1c} level, the slope for mean sensor glucose concentration (area under the curve) versus a centrally measured HbA_{1c} level was 24.4 mg/dL (1.36 mmol/L; 95% confidence interval, 22.0–26.7).

3 Individual variability ranged from sensor glucose concentrations of 128–187 mg/dL (7.1–10.4 mmol/L) for an HbA_{1c} level of 6.9–7.1% (52–54 mmol/mol).

4 The authors concluded that there is substantial individual variability between the measured versus calculated mean blood glucose concentrations.

Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Wilson DM, Xing D et al (2011) Hemoglobin A1c and mean glucose in patients with type 1 diabetes: analysis of data from the Juvenile Diabetes Research Foundation continuous glucose monitoring randomized trial. *Diabetes Care* **34**: 540–4

DIABETES CARE

Carb counting, glycaemic control and QOL in CSII

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 This 24-week study aimed to assess the effect of carbohydrate counting on glycaemic control and quality of life (QOL) in adults (n=61) with T1D on continuous subcutaneous insulin infusion (CSII) therapy.

2 Participants were randomised to either learning carbohydrate counting or traditional pre-meal insulin dose estimation. Biometric measurements were taken at 12 and 24 weeks.

3 In adults with T1D treated with CSII, carbohydrate counting was concluded to be well-tolerated and improve QOL, reduce BMI and waist circumference and, in per-protocol analysis, reduce HbA_{1c} levels.

Laurenzi A, Bolla AM, Panigoni G et al (2011) Effects of carbohydrate counting on glucose control and quality of life over 24 weeks in adult patients with type 1 diabetes on continuous subcutaneous insulin infusion: a randomized, prospective clinical trial (GIOCAR). *Diabetes Care* **34**: 823–7

BMJ

Overnight closed-loop insulin therapy

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓✓

1 The authors undertook two sequential, randomised, crossover studies to compare the safety and efficacy of overnight closed-loop insulin delivery with conventional insulin pump therapy.

2 Participants (n=24; 10 men) aged 18–65 years, and who had used insulin pump therapy for a minimum of 3 months, were enrolled.

3 Sensor-augmented pump therapy was used during overnight closed-loop delivery; conventional insulin pump settings were used during control nights.

4 One study compared closed-loop versus conventional therapy in 12 people after consuming a medium-sided meal (study A); the other compared closed-loop versus conventional therapy in 12 people after a larger meal with alcohol (study B).

5 The primary outcome was the time that plasma glucose levels were in the range 3.91–8.0 mmol/L.

6 Overnight closed-loop therapy in study A increased the time that plasma glucose levels were in target by a median 15% (P=0.002). For study B, this was increased by a median 28% (P=0.01)

7 Analysis of pooled data showed that closed-loop delivery increased time in plasma glucose target by a median 22% (P<0.001). Overnight time spent hypoglycaemic (plasma glucose <3.9 mmol/L) was reduced by a median 3% with closed-loop delivery (P=0.04).

8 The authors concluded that closed-loop delivery may improve overnight glycaemic control and reduce the risk of nocturnal hypoglycaemia in adults with T1D.

Hovorka R, Kumareswaran K, Harris J et al (2011) Overnight closed loop insulin delivery (artificial pancreas) in adults with type 1 diabetes: crossover randomised controlled studies. *BMJ* **342**: d1855

"Closed-loop delivery may improve overnight glycaemic control and reduce the risk of nocturnal hypoglycaemia in adults with T1D."