Technology

Sensor-augmented pump therapy effectively lowers HbA_{1c}

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The randomised controlled trials of sensor-augmented pump therapy (SAP) to date have failed to show a convincing added value from combining continuous glucose sensing with insulin pump therapy in terms of improving glycaemic control. This is either because of the trial design, for example comparing SAP with multiple daily injections (Bergenstal et al, 2010; Hermanides et al, 2011), or because a significant number of participants allocated to SAP did not use the sensor to the extent directed in the trial protocol (Raccah et al, 2009; Kordonouri et al, 2010); the latter studies have shown that if those failing to fulfil the study protocol in this way are excluded, SAP does appear to lower HbA_{1c} compared with pump therapy alone.

The SWITCH trial, reported by Battelino et al (2012; summarised alongside), overcomes the shortcomings of these previous trials. The study design is a randomised crossover, with participants having the sensor "on" for 6 months then "off" for 6 months following a 4-month washout, or *vice versa*; in this way participants act as their own controls. In total, 153 participants were randomised (81 adults and 72 children), all of whom had been using continuous subcutaneous insulin infusion (CSII) for at least 6 months but had never used continuous glucose sensing. To be eligible for the study and prior to each phase, participants had to take a test to demonstrate adequate understanding of diabetes, insulin pump therapy and continuous glucose monitoring.

SAP proved superior to CSII, with an HbA_{1c} lower by 4.7 mmol/mol (0.43%) on average while in the "sensor on" phase compared with the "sensor off" phase. Time spent with sensor glucose <3.9 mmol/L was significantly less during the "sensor on" compared with "sensor off" period, at 19 versus 31 minutes per day, respectively. However, severe hypoglycaemia and hypoglycaemia unawareness were exclusion criteria, and no significant difference was observed in episodes of severe hypoglycaemia between the two groups. Mean sensor use was 80%, which was sustained to the end of the "sensor on" period; 72% of the participants used the sensor at least 70% of the time. Unsurprisingly, those who used the sensor <70% of the time, compared with those who used it ≥70% of the time, showed a lesser reduction in HbA_{1c} (2.6 mmol/mol [0.24%] versus 5.6 mmol/mol [0.51%], respectively), but this was still statistically significant. In contrast to much of the evidence on the benefits of CSII, there was no correlation between baseline HbA_{1c} and HbA_{1c} reduction with the sensor "on".

During the "sensor on" phase there was a significant increase in the number of boluses given, as well as use of temporary basal rates, manual basal suspend function and the bolus wizard calculator. This is in keeping with observational data showing that usage of these is associated with better glycaemic control (Wilkinson et al, 2010).

The SWITCH study shows that anyone failing to achieve target HbA_{1c} on CSII may benefit from SAP, irrespective of their HbA_{1c} at the time. The use of testing to determine understanding of the various components of SAP may be beneficial in selecting individuals who will make best use of the technology irrespective of what proportion of time they deploy continuous glucose sensing; this may be a way of using SAP cost-effectively. In addition, optimising use of temporary basal rates and bolus insulin delivery before considering SAP is likely to be a cost-effective strategy. Unfortunately, we still await evidence that SAP or continuous glucose monitoring as a stand-alone intervention can have an impact on frequency of hypoglycaemia, despite experience with individual patients, and trials in those people at high risk of problem hypoglycaemia would be welcome.

Bergenstal RM, Tamborlane WV, Ahmann A et al (2010) Effectiveness of sensor-augmented insulin pump therapy in type 1 diabetes. *N Engl J Med* **363**: 311–20

Hermanides J, Nørgaard K, Bruttomesso D et al (2011) Sensor-augmented pump therapy lowers HbA_{1c} in suboptimally controlled type 1 diabetes. *Diabet Med* **28**: 1158–67

Kordonouri O, Pankowska E, Rami B et al (2010) Sensor-augmented pump therapy from the diagnosis of childhood type 1 diabetes. *Diabetologia* **53**: 2487–95

Raccah D, Sulmont V, Reznik Y et al (2009) Incremental value of continuous glucose monitoring when starting pump therapy in patients with poorly controlled type 1 diabetes. *Diabetes Care* **32**: 2245–50

Wilkinson J, McFann K, Chase HP (2010) Factors affecting improved glycaemic control in youth using insulin pumps. *Diabet Med* **27**: 1174–7

DIABETOLOGIA

CGM therapy in insulin pump-treated T1D improves glycaemic control

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

1 The authors investigated the effect of adding continuous glucose monitoring (CGM) to continuous subcutaneous insulin infusion (CSII) in children and adults with T1D with an HbA_{1c} level between 58.5 and 80.3 mmol/mol (7.5% and 9.5%).

2 Following a 1-month run-in phase when participants (n=153) were trained on CGM device use, they were randomised to either a "sensor on" (n=77) or a "sensor off" (n=76) study arm in a ratio of 1:1 for 6 months. Participants then crossed over to the other treatment arm following a 4-month washout period.

3 The difference in HbA_{1c} levels between the two study arms was measured after 6 months. Other outcomes included changes in the time spent in hypoglycaemia (<3.9 mmol/L), hyperglycaemia (>10 mmol/L) and euglycaemia (3.9–10 mmol/L), and changes in glycaemic patterns.

4 The mean HbA_{1c} level favoured the "sensor on" arm (64.34 mmol/mol [8.04%] versus 69.08 mmol/mol [8.47%], "sensor on" and "sensor off", respectively; P<0.001). When glucose sensing was suspended, glycaemic control reverted towards the baseline levels.

5 The "sensor on" period was associated with significantly less time spent in hypoglycaemia (P=0.009) and more daily insulin boluses (P<0.0001) than the "sensor off" period. The authors concluded that, in people with T1D using CSII, CGM is associated with decreased HbA_{1c} levels and reduced hypoglycaemia.

Battelino T, Conget I, Olsen B et al (2012) The use and efficacy of continuous glucose monitoring in type 1 diabetes treated with insulin pump therapy: a randomised controlled trial. *Diabetologia* **55**: 3155–62

CLINICAL ENDOCRINOLOGY (OXF)

CSII versus MDII: Glycaemic variability and GRP in T1D

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

1 The authors compared glycaemic variability, and whether this is associated with urinary F2-isoprostates and/or urinary PDF_{2alpha}, in children with T1D using either continuous subcutaneous insulin infusion (CSII) or multiple daily injection (MDI) therapy.

2 A total of 48 children underwent 3-day ambulatory continuous glucose monitoring (CGM) whilst using insulin pump therapy (n=22) or MDI (n=26).

3 Meals, sport activities and episodes of hypo- and hyperglycaemia were recorded. Urine samples were collected during two consecutive 24-hour periods.

4 After 72 hours, the monitor data were used to calculate parameters of glycaemic variability, the frequency of mild and severe hypoglycaemia and the glycaemic risk parameter (GRP; calculated using the glucose pentagon).

5 Compared with MDI, those on CSII had significantly lower insulin requirements, levels of high-density lipoprotein-cholesterol and mean of glycaemic excursions (P<0.01 for all comparisons) and the SD of mean glucose concentration (P<0.05). Mean blood glucose concentration and length and intensity of hyperglycaemic events were also lower in the CSII group.

6 Compared with healthy participants and those using MDI, the GRP was significantly lower in people using CSII (P<0.05). F2-isoprostates and PDF_{2alpha} were not associated with glycaemic variability parameters.

7 The authors concluded that, compared with MDI, CSII was associated with lower glycaemic variability and GRP in children with T1D.

Schreiver C, Jacoby U, Watzer B et al (2012) Glycaemic variability in paediatric patients with type 1 diabetes on continuous subcutaneous insulin infusion (CSII) or multiple daily injections (MDI): a cross-sectional cohort study. *Clin Endocrinol (Oxf)* 7 Nov [Epub ahead of print]

ENDOCRINE PRACTICE

U-500 insulin via CSII in T2D

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

1 The authors assessed the effects of U-500 insulin delivered via continuous subcutaneous insulin infusion (CSII) on HbA_{1c}, body weight, total delivery of insulin dose (TDID) and incidence of hypoglycaemia in 59 people with insulin-resistant T2D.

2 Participants were followed up at 3 months and then at 6-month intervals for a median of 49 months, and for up to 114 months.

3 At 3 months, average HbA_{1c} decreased significantly from a baseline value of 67 mmol/mol (8.5%) to 58 mmol/mol (7.5%; P<0.003); this improvement was sustained for >66 months of U-500 insulin use. People with higher baseline HbA_{1c} experienced greater reductions in HbA_{1c}.

4 There was no change in body weight or TDID over time. Weight correlated positively with TDID and severe hypoglycaemia was infrequent.

5 The authors concluded that U-500 insulin via CSII is safe and efficacious in people with insulin-resistant CSII.

Lane WS, Weinrib SL, Rappaport JM et al (2012) The effect of long-term use of U-500 Insulin via continuous subcutaneous insulin infusion on durability of glycemic control and weight in obese, insulin-resistant patients with type 2 diabetes. *Endocr Pract* 27 Nov [Epub ahead of print]

DIABETES CARE

RT-CGM versus SMBG in T2D

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

1 In this randomised controlled study, in people with T2D who were not taking prandial insulin, the authors compared real-time continuous glucose monitoring (RT-CGM; n=50) with self-monitoring of blood glucose (SMBG; n=50) over 12 months.

2 Raw RT-CGM data were analysed for response. Four common response patterns were identified: favourable response but high and variable glycaemia; worsening glycaemia; tight control; and incremental improvement.

3 At baseline, across response patterns and longitudinally, HbA_{1c}, glucose variability and engagement differed.

4 The authors concluded RT-CGM technology may be most effectively used in people with T2D and not on prandial insulin by targeting certain subgroups.

Fonda SJ, Salkind SJ, Walker MS et al (2012) Heterogeneity of responses to real-time continuous glucose monitoring (RT-CGM) in patients with type 2 diabetes and its Implications for application. *Diabetes Care* 19 Nov [Epub ahead of print]

DIABETES CARE

The smart CGM sensor concept

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

1 The smart continuous glucose monitor (sCGM) sensor output is connected to three real-time software modules for denoising, enhancement, and prediction of hypo- and hyperglycaemic events.

2 The authors assessed the performance of the sCGM using data from 24 people with T1D extracted from two trial databases.

3 The denoising module reduced the irregularity of the CGM time series by up to 57% (P<0.01). Accuracy was improved by the enhancement module, which reduced the absolute mean difference from 15.1% to 10.3%. Finally, hypo- and hyperglycaemic events were forecast an average 14 minutes ahead of time using the prediction module.

4 The authors concluded that the sCGM sensor has clinical utility in generating hypo- and hyperglycaemia alerts.

Facchinetti A, Sparacino G, Guerra S et al (2012) Real-time improvement of continuous glucose-monitoring accuracy: The smart sensor concept. *Diabetes Care* 19 Nov [Epub ahead of print]

> "Compared with multiple daily injections, continuous subcutaneous insulin infusion was associated with lower glycaemic variability and glycaemic risk parameter in children with T1D."