The Paradigm® Veo™ system: Reducing the duration and severity of hypoglycaemic episodes

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The Medtronic Paradigm® Veo™ system is unique amongst currently available pump systems in that it is the only system that features an automatic insulin suspend feature. The Veo™ system was introduced in the UK following failure to gain approval from the US Food and Drug Administration, who would not approve licensing of a medical device of this nature that could respond to changes in blood glucose levels without human intervention. As a result, to date there has been limited evidence published as to the true benefit of this system.

The principle of the low glucose suspend (LGS) is that when sensor-augmented pump users fail to respond to a hypoglycaemia alert, basal insulin delivery is suspended so that the duration of hypoglycaemia is reduced and recovery can occur in a timely fashion, even if no other intervention is forthcoming. Insulin suspension can last for up to 2 hours. If there follows a further 30 minutes of hypoglycaemia in which the user has again taken no action, another period of suspension will commence.

Published studies evaluating the impact of the LGS feature (Agrawal et al, 2011; Choudhary et al, 2011; Danne et al, 2011) indicate that there are several instances of LGS during the daytime but that these are generally short-lived. This suggests that these episodes are more the result of insulin-pump users consciously ignoring the hypoglycaemia warning alerts, rather than reflecting user unawareness due to hypoglycaemia severity. In contrast, overnight there are fewer but often much longer suspend episodes, which approach 2 hours each on average. When the suspend feature is used, the time spent in hypoglycaemia can be markedly reduced in those who are most susceptible.

The study by Garg et al (2012; summarised alongside) is novel in that the authors have specifically considered the utility of the LGS feature in reducing exercise-induced hypoglycaemia. The people studied did not have a history of severe hypoglycaemia, so should not have been unusually hypoglycaemia-prone, and would have been expected to respond to symptoms of hypoglycaemia with appropriate action. Nevertheless, when they used the LSG feature there was a significant reduction in hypoglycaemia duration, averaging more than 30 minutes. This was not associated with rebound hyperglycaemia, the mean end-of-study glucose in the LGS group being 5.1 mmol/L.

> *"The study by Garg et al is novel in that the authors have specifically considered the utility of the low glucose suspend feature in reducing exercise-induced hypoglycaemia."*

In conclusion, the outcomes of this study present the first evidence that the LGS feature could be beneficial to those with normal hypoglycaemia awareness who are not prone to severe hypoglycaemia. Reducing exercise-induced hypoglycaemia duration without requiring any intervention from the user would be expected to enhance quality of life and facilitate greater uptake of exercise opportunities in people with diabetes.

Agrawal P, Welsh JB, Kannard B et al (2011) Usage and effectiveness of the low glucose suspend feature of the Medtronic Paradigm Veo insulin pump. *J Diabetes Sci Technol* **5**: 1137–41

Choudhary P, Shin J, Wang Y et al (2011) Insulin pump therapy with automated insulin suspension in response to hypoglycemia: reduction in nocturnal hypoglycemia in those at greatest risk. *Diabetes Care* **34**: 2023–5

Danne T, Kordonouri O, Holder M et al (2011) Prevention of hypoglycemia by using low glucose suspend function in sensor-augmented pump therapy. *Diabetes Technol Ther* **13**: 1129–34

DIABETES TECHNOLOGY & THERAPEUTICS

The Medtronic Veo™ system: Effect on hypoglycaemia

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

1 The authors of this randomised crossover study evaluated the effect of the Medtronic Paradigm® Veo™ sensor-augmented insulin pump system on exercise-induced hypoglycaemic episodes in people with T1D aged 17–58 years (n=50).

2 All individuals had ≥3 months of experience using the Medtronic insulin pump system prior to study commencement. The pump featured a low glucose suspend (LGS), which stopped insulin delivery automatically for 2 hours at a glucose value of ≤3.88 mmol/L.

3 All people completed 134 exercise sessions with half of the cohort randomised to have the LGS either turned on (LGS-On) or off (LGS-Off; this subgroup received continuous insulin delivery regardless of sensor glucose).

4 Between-group hypoglycaemia severity and duration was compared using the YSI STAT Plus™ glucose and lactate analyser. In the LGS-On group, mean hypoglycaemia duration was significantly less (P=0.006) and mean nadir YSI glucose significantly higher (P<0.001) compared with the LGS-Off group. No rebound hyperglycamia was experience in the LGS-On group.

5 The authors concluded that sensor-augmented insulin delivery with LGS significantly reduced the duration and severity of hypoglycaemia in people with T1D, a common limit to intensification of glucose-lowering treatment.

Garg S, Brazg RL, Bailey TS et al (2012) Reduction in duration of hypoglycemia by automatic suspension of insulin delivery: the in-clinic ASPIRE study. *Diabetes Technol Ther* **14**: 205–9

DIABETES TECHNOLOGY & THERAPEUTICS

Modelling glucose metabolism in CSII-treated T1D

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

1 Algorithms modelling glucose control can be developed from mathematical models of glucose metabolism and are valuable in preclinical simulation research.

2 The study researchers investigated the effect of predetermined life events on blood glucose in people with insulin-pump-treated T1D (n=12).

3 Over 24 days, individuals were randomly assigned to complete two study days, separated by 3 weeks, during which they completed predetermined activities, including meals, insulin boluses and bouts of exercise.

4 Study days began at 08.00. The first event was a meal at 10.00, followed by 20 minutes of exercise or an insulin bolus at 12.30, and then, at 15.00, an exercise bout, insulin bolus or a snack. Blood glucose was stabilised at 17.00.

5 Throughout the study, people wore an insulin pump and either a continuous glucose monitor or activity monitor. Ten-minute plasma glucose measurements were recorded throughout the two intervention days. Following an event, plasma insulin and glucagon were analysed.

6 The study yielded high-quality information-rich data on fast and slow blood glucose changes following daily events in people with T1D. These outcomes can be used in the development of glucose control strategies.

Schmidt S, Finan DA, Duun-Henriksen AK et al (2012) Effects of everyday life events on glucose, insulin, and glucagon dynamics in continuous subcutaneous insulin infusion-treated type 1 diabetes: collection of clinical data for glucose modeling. *Diabetes Technol Ther* **14**: 210–7

ARCHIVES OF DISEASE IN CHILDHOOD

CSII therapy: 4-year efficacy and safety in children

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

1 The authors evaluated the 4-year safety and efficacy of continuous subcutaneous insulin infusion (CSII) in children with diabetes (n=67).

2 Baseline and CSII therapy follow-up data were collected on HbA_{1c}, height, weight, hypoglycaemia, insulin requirements and diabetic ketoacidosis.

3 At 6, 12, and 24 months, mean (±SD) HbA_{1c} decreased significantly from the pre-CSII level (P<0.01, P<0.01 and P<0.05, respectively). This trend continued until the study end but did not remain significant. CSII also significantly reduced insulin requirements (P<0.01).

4 A pre-school group (<6 years old) with 20 months' mean duration of CSII treatment (n=9) demonstrated a significant HbA_{1c} reduction (68 mmol/mol [8.4%] to 57 mmol/mol [7.44%], P<0.01) in the absence of severe hypoglycaemia.

5 The authors concluded that CSII therapy yields significant and sustained improvements in glycaemic control in children.

Hughes CR, McDowell N, Cody D et al (2012) Sustained benefits of continuous subcutaneous insulin infusion. *Arch Dis Child* **97**: 245–7

> *"At 6, 12, and 24 months, mean (±SD) HbA_{1c} decreased significantly from the pre-CSII level. This trend continued until the study end but did not remain significant."*

JOURNAL OF DIABETES SCIENCE AND TECHNOLOGY

Closed-loop insulin simulations predict clinical outcomes

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

1 The authors evaluated the ability of a low-order identifiable virtual patient (IVP) model to predict clinical outcomes for closed-loop insulin delivery in clinical subjects who were not used in model development.

2 The impact on HbA_{1c} of adding an insulin bolus to meals was assessed in a clinical paediatric cohort with T1D using the protocol reported in the Medtronic proportional-integral-derivative algorithm. The procedures were then reproduced in 10 "virtual" adults with T1D.

3 Peak postprandial glucose values and additional carbohydrate use were comparable in the clinical and IVP simulation groups.

4 The authors concluded that the closed-loop IVP model is highly predictive of clinical outcomes.

Kanderian SS, Weinzimer SA, Steil GM et al (2012) The identifiable virtual patient model: comparison of simulation and clinical closed-loop study results. *J Diabetes Sci Technol* **6**: 371–9

DIABETES TECHNOLOGY & THERAPEUTICS

CGM risk scores identify glucose variability

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

1 The aim of the study was to compare average daily risk range (ADRR) scores generated from continuous glucose monitoring (CGM; ADRRc) or glucose self-monitoring data (ADRRs) in measuring glucose variability in young children with T1D (n=48). ADRR scores were validated against mean amplitude of glycaemic excursion (MAGE) scores.

2 The mean ADRRc score was significantly higher than the ADRRs score (P<0.001), demonstrated a higher risk for glucose excursion, and was more strongly correlated with the MAGE score.

3 The authors concluded that, compared with the ADRRs score, the ADRRc score measures glucose variability more sensitively in children.

Patton SR, Midyett LK, Dolan LM et al (2012) A comparison of average daily risk range scores for young children with type 1 diabetes mellitus using continuous glucose monitoring and self-monitoring data. *Diabetes Technol Ther* **14**: 239–43