DIABETIC MEDICINE

Sitagliptin improves glycaemic control in adults with T1D

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

1 This 8-week, randomised, cross-over study assessed the potential use of the dipeptidyl peptidase-4 (DPP-4) inhibitor sitagliptin to decrease postprandial rises in glucagon in adults with T1D.

2 Participants were randomised to either sitagliptin 100 mg/day or placebo for 4 weeks and then crossed over.

3 Sitagliptin was found to significantly reduce both 2-hour postprandial and 24-hour area under the curve blood glucose levels, despite a reduction in the total and prandial insulin dose.

4 Data obtained from continuous glucose monitoring showed that sitagliptin improved measures of glycaemic control, including mean blood glucose levels (–0.6 mmol/L) and the time spent in the euglycamic range of 4.4–7.8 mmol/L (0.4±0.2 hours; P=0.046).

5 Significant reductions in the Glycaemic Risk Assessment Diabetes Equation (GRADE), M100 and J-index were also observed.

6 Significant reductions in the levels of HbA_{1c} were observed in the sitagliptin group (–2.91±1.16 mmol/mol [–0.27±0.11%]; P=0.025) after controlling for period, treatment and insulin dose.

7 It was concluded that sitagliptin significantly improved both postrandial and 24-hour glycaemic control in adults with T1D, while significantly reducing prandial insulin requirements.

Ellis SL, Moser EG, Snell-Bergeon JK et al (2011) Effect of sitagliptin on glucose control in adult patients with Type 1 diabetes: a pilot, double-blind, randomized, crossover trial. *Diabet Med* **28**: 1176–81

DPP-4 inhibitors: First evidence for use in T1D?

Adrian Scott, Consultant Physician in Diabetes and General Medicine, Northern General Hospital, Sheffield

I have spent the past two decades trying to persuade people with type 1 diabetes (T1D) to:

a. Inflict pain on themselves with finger-prick tests at least four-times daily.
b. Anticipate how many chips they are going to eat during the next meal.
c. Calculate how many units of insulin they will need to account for those chips (as well as "correcting" the dose to account for the cock-up they made estimating how much carbohydrate was in the last meal).
d. Inject this precisely calculated dose of insulin into a virgin piece of subcutaneous tissue exactly 20 minutes before their first mouthful.
e. Exercise regularly (but only if they have taken this into account before injecting the precisely calculated amount of insulin).

However, what I actually wanted to do was give them a pancreas that worked, or the mechanical equivalent. Until that happens, I will have to continue tinkering, by trying to make sense of what actually has gone wrong with their pancreas.

It is easy to forget the differences between T1D and type 2 diabetes (T2D). While the logic of enhancing glucagon-like peptide-1 (GLP-1) release is relatively easy to understand for someone with T2D, it is less obvious in those with T1D. The loss of the paracrine effects between the alpha- and beta-cells of the pancreas in T1D results in uncontrolled glucagon release, which partly accounts for the greater blood glucose fluctuations in people with T1D compared with those in people with T2D.

The study by Ellis et al (2011; summarised alongside) has demonstrated a small but significant benefit from modulating GLP-1 action in people with T1D through the addition of the dipeptidyl peptidase-4 (DPP-4) inhibitor sitagliptin. This oral therapy – most notably used in the management of T2D – decreased postprandial glucagon rises, thereby improving postprandial and 24-hour blood glucose levels, as well as reducing prandial insulin requirements.

It may not be a new pancreas, but it does open the way to testing other incretin mimetics in this population (don't you ever wish you'd been a cardiologist?).

DIABETIC MEDICINE

CSII associated with improved behaviour in children with T1D

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

1 The authors of this study aimed to establish whether there was any association between continuous subcutaneous insulin infusion (CSII) therapy and sustained improvements in behaviour and glycaemic control in children with T1D.

2 Twenty-seven children with T1D aged 8–18 years who had been assessed prior to commencing CSII therapy were re-evaluated 6–8 weeks later, and then again after 2 years.

3 HbA_{1c} levels were measured, and behaviour was assessed using the Behavioural Assessment System for Children – 2nd edition (BASC-2).

4 Parent-reported internalising and externalising levels were significantly lower after 2 years of CSII therapy compared with pre-CSII levels; no significant difference was observed for self-reported internalising and externalising levels.

5 No significant difference was observed with HbA_{1c} levels, despite an initial improvement at 6–8 weeks.

6 The authors concluded that children with T1D displayed sustained improvements in parent-reported behaviour, but not in self-reports of behaviour or glycaemic control at 2 years.

Knight SJ, Northam EA, Cameron FJ, Ambler GR (2011) Behaviour and metabolic control in children with type 1 diabetes mellitus on insulin pump therapy: 2-year follow-up. *Diabet Med* **28**: 1109–12

"Healthcare professionals need to balance their aims for otimal glycaemic control with realism and appreciation of their patients' efforts."

DIABETIC MEDICINE

Users' experiences vital in developing paediatric care

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

1 As part of the DEPICTED (Development and Evaluation of a Psychosocial Intervention for Children and Teenagers Experiencing Diabetes) study, the authors sought to describe users' experiences of paediatric care to help inform the development of an intervention to improve communication between healthcare staff and patients.

2 Six audio-recorded focus discussion groups were set up (n=32) and the recordings were transcribed; notes were coded thematically and analytical themes developed.

3 Three main themes developed: the lack of two-way conversation regarding glycaemic control in the clinic setting; the restricting experience of living with diabetes; and the difficult interactions around diabetes the children had with their schools.

4 Children and their parents felt that doctors in particular were seen as struggling to link these themes of everyday life in their consultations. Moreover, children felt marginalised in clinics, despite active involvement in their own blood glucose management at home.

5 The authors concluded that healthcare professionals need to balance their aims for otimal glycaemic control with realism and appreciation of their patients' efforts.

Hawthorne K, Bennert K, Lowes L et al (2011) The experiences of children and their parents in paediatric diabetes services should inform the development of communication skills for healthcare staff (the DEPICTED Study). *Diabet Med* **28**: 1103–8

DIABETES

Rituximab selectively suppresses specific islet antibodies

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

1 The authors of this study (the TrialNet Anti-CD20 Study Group) aimed to evaluate the effect the beta-cell-depleting monoclonal antibody rituximab on multiple islet auto-antibodies in people with new-onset type 1A diabetes (T1AD).

2 In their previous study, the authors showed that rituximab decreased the loss of C-peptide over the first year of follow-up and markedly depleted B lymphocytes for 6 months after administration.

3 Participants (n=87; aged 8–40 years received either rituximab or placebo weekly for four doses close to the onset of T1AD. Autoantibodies to insulin (IAAs), GAD65 (GADAs), insulinoma-associated protein 2 (IA2As), and ZnT8 (ZnT8As) were measured.

4 Rituximab was found to markedly suppressed IAAs compared with placebo, although the intervention had a much smaller effect on GADAs, ZnT8As and IA2As. Forty per cent of participants treated with rituximab who were IAA positive became IAA negative versus 0 of 29 from the placebo group (P<0.0001).

5 A subgroup of six people were treated within 50 days of T1AD; in these people, rituximab markedly suppressed IAAs in all participants for 1 year, and for 3 years in four people, despite continuing insulin therapy.

6 The mean level of IAAs at study entry, independent of rituximab treatment, was significantly lower (P=0.035) for those who maintained C-peptide levels during the first year of follow-up in both the rituximab and placebo group.

7 It was concluded that studies in pre-diabetic non-insulin-treated people are required to evaluate the specific effects of rituximab on IAA levels.

Yu L, Herold K, Krause-Steinrauf H et al (2011) Rituximab selectively suppresses specific islet antibodies. *Diabetes* **60**: 2560–5

DIABETIC MEDICINE

Expert statement on preventing T1D

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

1 In October 2011, a panel of European experts met to review strategies for the prevention of T1D, examining: T1D epidemiology; possible underlying mechanisms of the continuous and rapidly increasing incidence of T1D at younger ages; previous trials data looking into prevention of the condition.

2 Three consensus recommendations arose; these are discussed below.

3 First, resources such as national diabetes registries and natural history studies were identified as playing a vital role in the development and refinement of techniques used in screening for T1D risk factors.

4 Second, the panel highlighted the importance of dissecting out the earliest physiological events after birth, as well as environmental factors that might affect such phenotypes, to facilitate a mechanistic approach to designing future research.

5 Third, it was noted that current interventions at later stages of disease have relied mainly on non-antigen-specific mechanisms. The panel recommended that for primary prevention, interventions must be based on knowledge of the actual disease process such that: trial participants would be stratified according the disease-associated molecular phenotypes; the autoantigen(s) and immune responses to them; and the manipulation of the environment, as early as possible in life.

6 Finally, it was recommended that combinations of interventions should be considered as they may allow targeting different components of disease, thus lowering side-effects while increasing efficacy.

Todd JA, Knip M, Mathieu C (2011) Strategies for the prevention of autoimmune type 1 diabetes. *Diabet Med* **28**: 1141–3

"Although paternal involvement was not directly associated with treatment adherence, it was associated with poorer glycemic control."

MEDICAL CARE

Health utilities for children and adults with T1D

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

1 This study aimed to understand potential differences in quality of life (QOL) as a function of age, type of respondent (self-report versus proxy report), and method of assessment (direct versus indirect) in people with T1D.

2 Self-reported health utilities were taken for 213 adults and 238 children with T1D, and 223 by parent proxy report for overall QOL (Health Utilities Index [HUI] Mark 3 and experienced time-trade-off [TTO] questions) and hypothetical complication states (TTO questions).

3 The mean health utility value for overall QOL ranged from 0.81 to 0.91. Children were found to have a significantly higher overall QOL compared with adults (0.89 vs 0.85; $P<0.01$) by HUI; the difference in QOL by TTO was not significant.

4 No significant differences in QOL were observed between child self-report and parent proxy report. Moreover, health utilities were significantly higher for HUI versus TTO for parent proxy report ($P<0.01$) but not for adult or child self-report.

5 Health utility values for complication states (hypothetical) were lower than for current QOL: values were lower for stroke (0.34–0.53), end-stage renal disease (0.47–0.55), and blindness (0.52–0.69) than for amputation (0.73–0.82) and angina (0.74–0.80).

6 The authors concluded that differences in health utilities by age, self-report versus proxy report, and method, raise important questions about whose utilities should be used in economic analyses.

Lee JM, Rhee K, O'grady MJ et al (2011) Health utilities for children and adults with type 1 diabetes. *Med Care* **49**: 924–31

DIABETIC MEDICINE

Sensor-augmented CSII improves HbA_{1c} in people with poorly controlled T1D

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

1 This investigator-initiated multi-centre trial (the Eurythmic Trial) was undertaken to assess the efficacy of sensor-augmented continuous subcutaneous insulin infusion (CSII) therapy versus multiple-daily injection (MDI) therapy in people with T1D with sub-optimal glycaemic control.

2 Participants with T1D ($n=83$; 40 women; age 18–65 years; HbA_{1c} level ≥65 mmol/mol [≥8.2%]) on MDI therapy were randomised to 26 weeks' treatment with either sensor-augmented CSII therapy ($n=44$) or continuation of their MDI regimen ($n=39$).

3 In the sensor-augmented CSII group, mean HbA_{1c} level changed from 69 mmol/mol (8.46%) at baseline to 56 mmol/mol (7.23%) at 26 weeks, compared with 70 mmol/mol (8.59%) to 69 mmol/mol (8.46%), respectively, in the MDI group.

4 By week 26, the mean difference in HbA_{1c} change was –1.21% (95% confidence interval, –1.52 to –0.90; $P<0.001$) in favour of the sensor-augmented CSII group, which was achieved without an increase in time spent in hypoglycaemia.

5 Four episodes of severe hypoglycaemia occurred in those on sensor-augmented CSII and one episode in those on MDI therapy ($P=0.21$).

6 Patient-reported outcomes improved in the sensor-augmented CSII group.

7 It was concluded that sensor-augmented CSII therapy effectively lowers HbA_{1c} levels in people with T1D suboptimally controlled with MDI therapy.

Hermanides J, Nørgaard K, Bruttomesso D et al (2011) Sensor-augmented pump therapy lowers HbA(1c) in suboptimally controlled Type 1 diabetes; a randomized controlled trial. *Diabet Med* **28**: 1158–67

JOURNAL OF PEDIATRIC PSYCHOLOGY

Paternal involvement associated with glycaemic control

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

1 Fathers are an important but understudied influence on the management of children with diabetes.

2 In this study, the authors sought to examine the relationship of paternal involvement in their preadolescent's T1D care with treatment adherence and glycaemic control.

3 A total of 136 mothers and fathers of pre-adolescents (aged 9–12 years) with T1D were recruited to report on paternal involvement in their child's diabetes care. Treatment adherence was measured by interview and blood glucose meter data.

4 The ratings given by mothers and fathers for their involvement in diabetes care were compared, and three structural equation models were evaluated to link paternal involvement with treatment adherence and glycemic control.

5 Similar amounts of paternal involvement were reported by mothers and fathers, although mothers rated paternal involvement as more helpful. The results supported a model that indicates links between more paternal involvement and higher HbA_{1c} and between lower treatment adherence and higher HbA_{1c}. Mediation and moderation models, however, were not supported.

6 The authors concluded that although paternal involvement was not directly associated with treatment adherence, it was associated with poorer glycemic control, and that some fathers may increase their involvement in response to poor glycemic control.

Hilliard ME, Rohan JM, Carle AC et al (2011) Fathers' involvement in preadolescents' diabetes adherence and glycemic control. *J Pediatr Psychol* **36**: 911–22