Management of type 1 diabetes

More tools in the insulin toolbox

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Without doubt, diet and insulin are, along with exercise, the cornerstones of type 1 diabetes management. The tools, such as insulin, have undoubtedly become more predictable in their speed and duration of action. The glycaemic impact of different foodstuffs alone and in combination with others has been the subject of intense scrutiny for many years. The problem has always been trying to match insulin dose, speed of onset and duration of action, with postprandial blood glucose levels.

In days gone by, carbohydrate portions were prescribed to match the insulin dose (woe betide the Shredded Wheat biscuit that I have seen beheaded by overzealous dietitians to make it a 10-gram rather than 15-gram portion of carbohydrate). Now, of course, DAFNE (Dose Adjustment For Normal Eating) or BERTIE (Bournemouth Type 1 Intensive Education) programmes allow unrestricted access to carbohydrate, provided that the quantity has been counted and this converted to the appropriate dose of insulin. The problem is that, for many, mathematics education stopped around the age of 16 years and multiplication is thought to be something only rabbits do. Fortunately, in this technological age, a string of devices known as "automated bolus calculators" (ABCs) are available to electronically calculate insulin bolus doses to address carbohydrate intake and out-of-range blood glucose levels. In the study by Zisser et al (2010; summarised alongside), three such devices were compared with differing results due largely to the different algorithms used by the devices. In the study by Maurizi et al (2011; summarised below), use of the device was both practical and resulted in improved glycaemic control.

Nevertheless, using these devices routinely requires a degree of obsessive-compulsion not seen in all people with diabetes. For those who are willing and able, however, they bring much needed precision to the complex business of insulin dosing. They can help people with diabetes get the best out of their insulin toolbox.

Other interesting summaries in this section are by Gupta et al (2011) and Pettis et al (2011; both summarised overleaf), on the advantages of intradermal versus subcutaneous insulin injection. Further studies are required but it would appear that intradermal injections using microneedle technology significantly improve insulin absorption and reduce postprandial glucose excursions.

DIABETES TECHNOLOGY & THERAPEUTICS

New bolus calculator, Calsulin, improves glycaemic control

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

1 A new bolus calculating tool, Calsulin (Thorpe Products, Cambridge), was tested by 40 people with T1D (aged 18–65 years).

2 At baseline, HbA_{1c} levels were 7.9±1.0% (63±10.9 mmol/mol) in the Calsulin treated group and 7.8±1.6% (62±17.5 mmol/mol) in the control group.

3 In the Calsulin group, HbA_{1c} levels improved slightly after 3 months and significantly at 6 months compared with the control group (–0.85% vs –0.07% [–9.3 vs –0.8 mmol/mol]; $P<0.05$).

4 The authors concluded that Calsulin improved glycaemic control and is a helpful tool for calculating bolus doses for people with T1D.

Maurizi AR, Lauria A, Maggi D et al (2011) A novel insulin unit calculator for the management of type 1 diabetes. *Diabetes Technol Ther* **13**: 425–8

DIABETES TECHNOLOGY & THERAPEUTICS

Comparison of three bolus calculators

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

1 Automated bolus calculators (ABCs) are now provided within insulin pump systems that automatically calculate bolus doses based on carbohydrate intake and previous insulin doses.

2 The efficacy of three ABCs were compared: the AccuChek® Combo (Roche, Fishers, Indiana); the Animas® 2020 (West Chester, Pennsylvania); and the MiniMed Paradigm Bolus Wizard® (Medtronic, Northridge, California).

3 A total of 24 people with T1D took part in this prospective triple cross-over trial, each using one ABC at a time in a random order.

4 The calculated bolus dose was reduced by 25% to induce postprandial hyperglycaemia and 2 hours after a meal the ABCs were allowed to determine whether a correction dose was needed.

5 Mean differences in 6-hour blood glucose levels following a test meal were taken; difference of mean results from the target (6.1 mmol/L) were: 2.6±1.8 mmol/L for the Medtronic device; 0.9±1.7 mmol/L for the Animas device and 1.0±1.9 mmol/L for the Roche device.

6 The Roche and Animas devices advised a correction bolus dose significantly ($P=0.0001$ and $P=0.0002$, respectively) more often than the Medtronic device.

7 It was concluded that the Roche and Animas ABCs were more efficacious than the Medtronic device, which may be due to the different setups and algorithms.

Zisser H, Wagner R, Pleus S et al (2010) Clinical performance of three bolus calculators in subjects with type 1 diabetes mellitus: a head-to-head-to-head comparison. *Diabetes Technol Ther* **12**: 955–61

"Intradermal infusion of insulin using microneedles has the potential to improve diabetes management."

DIABETES TECHNOLOGY & THERAPEUTICS

Postprandial BG levels improved with intradermal insulin injection compared with subcutaneous

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

1 The pharmacodynamics and pharmacokinetics of intradermal infusion in people with T1D by microneedle versus subcutaneous delivery were assessed in this study.

2 A total of 29 people participated in the five-way crossover study, where insulin lispro or regular human insulin was administered via 8-mm syringe needle or 1.5-mm steel microneedle.

3 Both insulin lispro and human insulin were administered at 2 minutes and 17 minutes before a standardised 82-g carbohydrate meal by both subcutaneous injection and intradermal microneedle.

4 The 90-minute postprandial blood glucose level for intradermal injection of regular human insulin was 14% lower than subcutaneous insulin injection with regular human insulin at 17 minutes before the meal ($P<0.0001$) and 11% lower than intradermal human insulin at 2 minutes ($P=0.0006$).

5 Both intradermal administrations demonstrated significantly faster uptake and time to maximum concentration, higher maximum concentration and shorter systemic circulating duration compared with subcutaneous administration.

6 The authors concluded that postprandial blood glucose levels with human insulin microneedle administration were improved compared with subcutaneous injection when administered 17 minutes prior to a meal.

Pettis RJ, Hirsch L, Kapitza C et al (2011) Microneedle-based intradermal versus subcutaneous administration of regular human insulin or insulin lispro: pharmacokinetics and postprandial glycemic excursions in patients with type 1 diabetes. *Diabetes Technol Ther* **13**: 443–50

DIABETES TECHNOLOGY & THERAPEUTICS

Pharmacokinetics of intradermal infusion of insulin with a microneedle

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

1 A 0.9 mm-long microneedle has been developed for the intradermal infusion of insulin. The pharmacokinetics, postprandial glycaemic response and pain associated with this needle were compared with a standard 9-mm catheter.

2 On separate occasions, five people with T1D received a bolus dose of insulin lispro by microneedle or by subcutaneous catheter followed by a meal.

3 It took half the time for insulin concentrations to reach peak levels with the microneedle than with the subcutaneous catheter and the microneedle led to greater reduction in plasma glucose levels. It was also significantly less painful than the catheter ($P=0.02$).

4 It was concluded that intradermal infusion of insulin using microneedles has the potential to improve diabetes management.

Gupta J, Felner EI, Prausnitz MR (2011) Rapid pharmacokinetics of intradermal insulin administered using microneedles in type 1 diabetes subjects. *Diabetes Technol Ther* **13**: 451–6

DIABETIC MEDICINE

Sensor-augmented pump therapy improves HbA_{1c} level

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

1 This 26-week trial compared sensor-augmented insulin pump therapy with multiple daily injections (MDI).

2 A total of 83 people with T1D were randomised to receive treatment with sensor-augmented insulin pump therapy (Paradigm REAL-Time [Medtronic, Northridge, California]; $n=44$) or continue with MDI ($n=39$).

3 Mean HbA_{1c} level improved in the sensor-augmented group from 8.5% (69 mmol/mol) at baseline to 7.2% (56 mmol/mol) at 26 weeks, and from 8.6% (70 mmol/mol) to 8.5% (69 mmol/mol) in the MDI group.

4 The mean difference between groups was –1.21% (95% confidence interval, 1.52 to –0.90; $P<0.001$) in favour of the sensor-augmented group.

5 Sensor-augmented insulin pump therapy was found to improve HbA_{1c} levels in this cohort with T1D.

Hermanides J, Nørgaard K, Bruttomesso D et al (2011) Sensor-augmented pump therapy lowers HbA1c in suboptimally controlled type 1 diabetes; a randomized controlled trial. *Diabet Med* [Epub ahead of print]

DIABETIC MEDICINE

Impact of high- and low-GI meals on blood glucose levels

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

1 The impact of high- and low-glycaemic index (GI) foods was assessed in 16 people with T1D treated with continuous subcutaneous insulin infusion.

2 Blood glucose levels after the low-GI meal were significantly lower than after the high-GI meal ($P<0.05$ to $P<0.01$).

3 The area under the curve after the low-GI meal was 20% lower than after the high-GI meal ($P=0.006$).

4 Meals with different GI were found to produce different postprandial blood glucose levels despite having the same carbohydrate content.

Parillo M, Annuzzi G, Rivellese AA et al (2011) Effects of meals with different glycaemic index on postprandial blood glucose response in patients with type 1 diabetes treated with continuous subcutaneous insulin infusion. *Diabet Med* **28**: 227–9

DIABETES RESEARCH AND CLINICAL PRACTICE

HbA_{1c} level at diagnosis correlates with future glycaemic control

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

1 The relationship between HbA_{1c} level at diagnosis and future glycaemic control was assessed in 120 children with T1D.

2 People <18 years of age who had an HbA_{1c} level taken at diagnosis and at least one HbA_{1c} level during follow-up were included.

3 Mean age at diagnosis was 7.6±3.9 years and mean HbA_{1c} level was 10.9±1.9% (96.0±20.8 mmol/mol).

4 Baseline characteristics examined included age, race, sex, symptom duration and anthropometrics.

5 HbA_{1c} level at diagnosis correlated with symptom duration, age at diagnosis and HbA_{1c} level at 3 years (r=0.29; P<0.01). HbA_{1c} level at 1 year was highly correlated with HbA_{1c} level at 2-year follow-up (r=0.61; P<0.001) and 4-year follow-up (r=0.31; P<0.001).

6 HbA_{1c} level at diagnosis and 1 year after diagnosis was related to future glycaemic control in children newly diagnosed with T1D.

7 The authors concluded that identifying children with T1D who may benefit from intensification of diabetes care can be undertaken using 1-year HbA_{1c} levels as a guide.

Viswanathan V, Sneeringer MR, Miller A et al (2011) The utility of hemoglobin A1c at diagnosis for prediction of future glycemic control in children with type 1 diabetes. *Diabetes Res Clin Pract* **92**: 65–8

DIABETES TECHNOLOGY & THERAPEUTICS

Sensors improve glycaemic control

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

1 Sensor-augmented insulin pump therapy was compared with standard insulin pump therapy in children with T1D.

2 HbA_{1c} level improved for all children but the improvement was significantly greater for sensor-augmented insulin pump therapy users (P=0.005).

3 It was concluded that use of sensors with insulin pump therapy can improve glycaemic control more than pump therapy alone.

Scaramuzza AE, Iafusco D, Rabbone I et al (2011) Use of integrated real-time continuous glucose monitoring/insulin pump system in children and adolescents with type 1 diabetes: a 3-year follow-up study. *Diabetes Technol Ther* **13**: 99–103

"Use of sensors with insulin pump therapy can improve glycaemic control more than pump therapy alone."