

Modern strategies for management of glycaemia in type 1 diabetes

Sankalpa Neupane
Mark L Evans

Abstract

The last decade has seen significant advances in the management of type 1 diabetes mellitus. The usual management of type 1 diabetes involves 'physiological' basal bolus regimens with multiple daily insulin injections. Structured education programmes are of great importance in realizing the potential of the flexible insulin regimens that are now technically possible. These offer individuals with type 1 diabetes standardized support and education in counting carbohydrates (and perhaps fat and protein) and in adjusting doses for other behavioural factors. Use of technology such as insulin pumps (continuous subcutaneous insulin infusion) and continuous glucose monitoring is growing. Increasingly, systems are becoming available that link continuous glucose monitoring to insulin pumps, thus allowing automation of at least some aspects of insulin delivery. Data from many devices – meters, pumps and continuous glucose monitors – are downloadable and can be analysed and/or shared with healthcare providers. In this chapter, we describe how modern glucose monitoring and insulin replacement can be used strategically with education to manage glucose levels in type 1 diabetes.

Keywords Continuous glucose monitoring; continuous subcutaneous insulin infusion; hypoglycaemia; insulin pumps; islet transplantation; MRCP; pancreas transplantation; structured education

Introduction

Many technical and healthcare changes have occurred over the last few years in type 1 diabetes mellitus (T1DM). New insulin analogues (either engineered to act more rapidly or be longer lasting) continue to be developed and have been widely adopted in T1DM. The combination of rapid-acting 'bolus' insulin, given before meals and/or as *ad hoc* doses to correct high blood glucose values, with long-acting background insulin replacement (by convention termed 'basal' if delivered by insulin pump) allows patients to use more 'physiological' basal bolus insulin regimens (Figure 1).

Sankalpa Neupane MBBS MRCP is a Consultant in Diabetes and Endocrinology at the Norfolk and Norwich University Hospital NHS Trust, UK. Competing interests: none declared.

Mark L Evans MD FRCP is a University Lecturer/Honorary Consultant at Wellcome Trust/MRC Institute of Metabolic Science, University of Cambridge and Cambridge University Hospitals (Addenbrooke's), UK. Competing interests: none declared.

Key points

- Structured education should be a keystone of management, giving patients the skill set to adjust insulin doses flexibly around food and lifestyle
- Insulin pumps are increasingly popular as an alternative to multiple daily injections, although they are used by <25% of individuals with type 1 diabetes in the UK
- Continuous and flash glucose monitoring are available and increasing in use as accuracy and 'usability' improve
- Insulin pumps and continuous glucose monitoring can be coupled to automate insulin delivery
- Pancreas and islet cell transplantation may give insulin independence but are reserved for individuals with complications and/or hypoglycaemia

Structured patient education

The flexibility offered by modern variable insulin regimens presents a challenge for patients, who need to learn and use many self-management skills beyond simply checking blood glucose concentration and administering insulin. For example, many people with T1DM adjust doses of mealtime rapid-acting insulin depending on the carbohydrate content of their food, meaning that they need training to count carbohydrates accurately. Evidence-based structured educational packages have emerged in the UK over the last decade. The largest and best established of these is DAFNE (Dose Adjustment for Normal Eating), described below, but a number of broadly similar smaller structured education programmes are also used in UK services.

DAFNE is based on a patient education model developed in Düsseldorf. In a randomized controlled trial, DAFNE improved blood glucose control and patient well-being.¹ It was introduced as a clinical service in the UK in 2002. By June 2014, 75 centres in the UK and Ireland were delivering DAFNE to 31,000 patients and growing at a rate of 4000–5000 patients per annum. It has also been adopted in Australia, New Zealand and Singapore. DAFNE continues to be effective, with improved glycaemic and patient-reported outcomes.² Patients experience not only lower average blood glucose concentrations, reflected by lower glycated haemoglobin (HbA_{1c}) values, but also less hypoglycaemia and an improvement in their ability to detect a falling blood glucose sooner.

DAFNE and similar programmes provide education in the skills required to self-adjust insulin doses; these include carbohydrate counting (Figures 2 and 3) and adjustment for exercise/activity, illness, stress, alcohol, travel and the menstrual cycle. The DAFNE approach teaches patients to count carbohydrate intake in 10 g portions and then apply an individualized insulin:carbohydrate ratio to calculate prandial insulin. Other programmes may also use portions (for simplicity) or grams of carbohydrate. DAFNE is delivered in group sessions over 5 days.

In common with the Düsseldorf programme, DAFNE also has a supporting structure with a clear philosophy, written

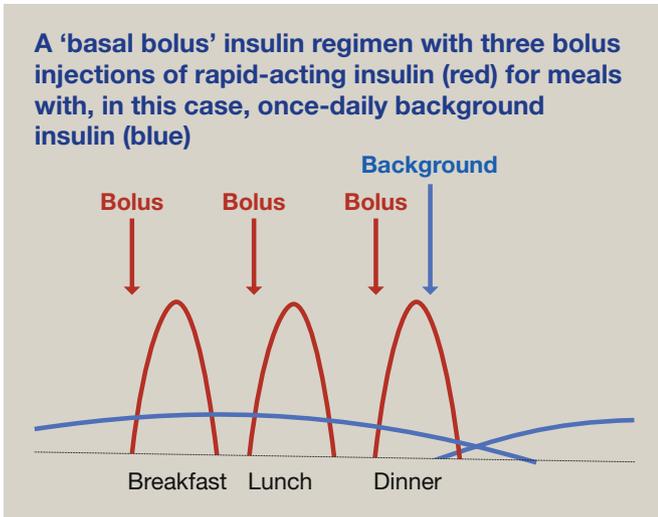


Figure 1

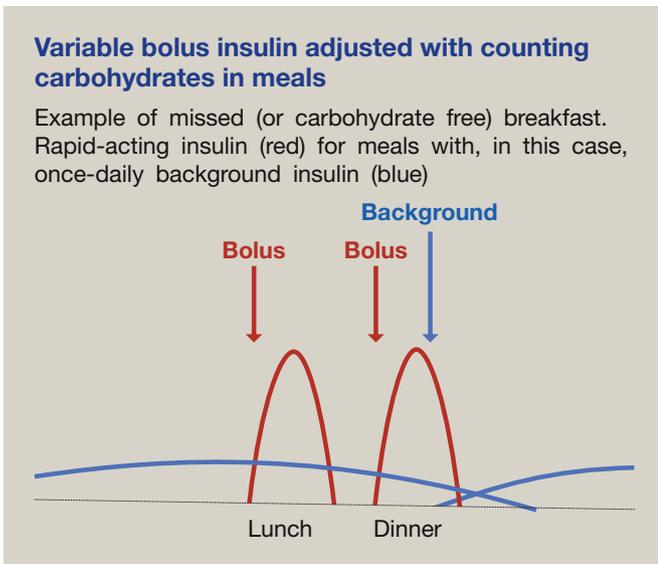


Figure 2

curriculum, processes for training and accrediting educators, quality assurance process including regular external peer review and audit of process and outcomes, and an anonymized database. Patient education also highlights the increasing role of non-medical staff as part of a multidisciplinary team approach, with specialist nurse educators and diabetes dietitians being highly trained and skilled in delivering and supporting education.

Structured educational packages also exist for children/adolescents with T1DM although the evidence base is not as established as in adults.

Continuous subcutaneous insulin infusion (CSII; 'insulin pumps')

With CSII, a rapid-acting insulin is pumped in constantly as a basal insulin replacement via an indwelling subcutaneous infusion cannula, self-inserted typically into the abdomen, buttock, thigh or arm. Patients can then use the pump to deliver an insulin bolus to cover meals and/or corrections for high glucose values

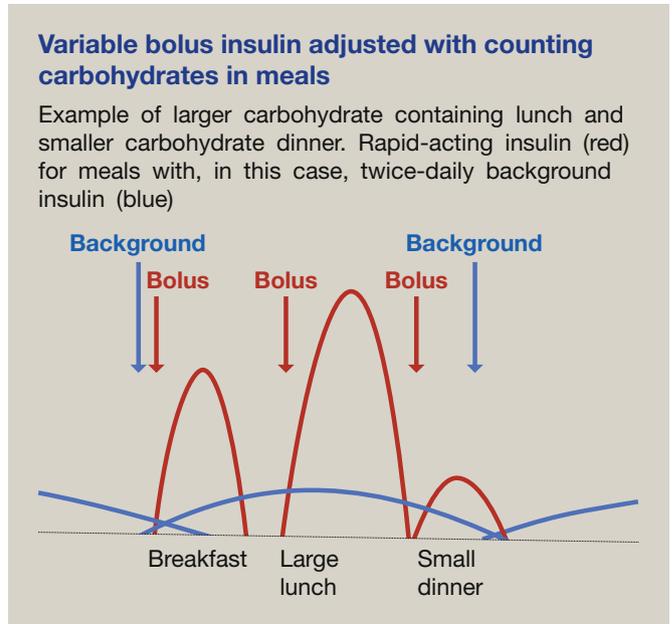


Figure 3

as needed (Figure 4). Typically every 3 days, the infusion set is removed and a fresh set inserted at a different site.

Early CSII models were cumbersome and unreliable, but the last decade has seen increased uptake in many developed countries in both children and adults. Used judiciously, CSII can improve glucose control,³ but these systems are currently more complex technically and medically so are unlikely to fully replace injections as standard treatment for insulin-requiring diabetes in the near future.

Particular advantages of modern pumps over multiple daily injections are:

- the ability to pre-programme variable basal insulin delivery – useful for patients with marked circadian variability in insulin requirements

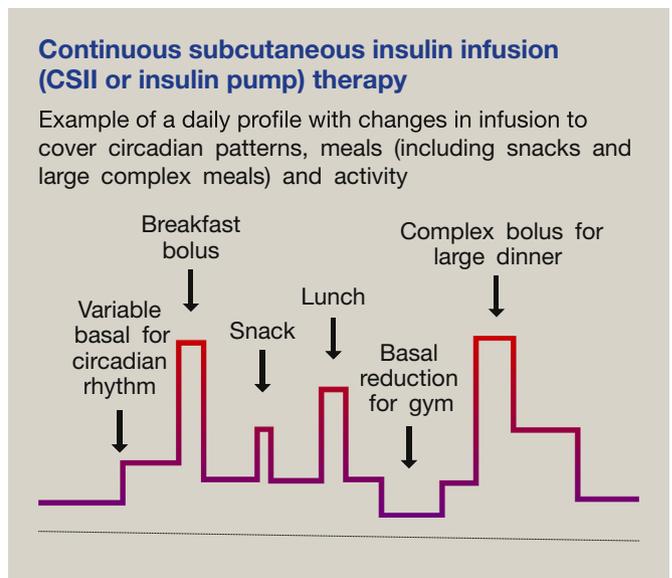


Figure 4

- temporary basal rates, where basal insulin delivery can be adjusted for a defined period of time – especially useful for lowering insulin delivery with unplanned or unexpected activity to reduce risk of hypoglycaemia
- the delivery of small amounts of insulin accurately – useful for children and some adults with low insulin requirements in whom it is difficult to deliver small doses accurately with injections
- complex bolus options, allowing mealtime insulin delivery to be extended over a protracted time period – useful for slowly absorbed foods (e.g. large meals with mixed carbohydrates and fat slowing absorption, such as pizza) or in patients with diabetic gastroparesis
- bolus-calculating software, which calculates a suggested insulin dose from patient-specific indices such as carbohydrate:insulin ratio and insulin sensitivity factors – the latter feature can remove some of the potential for arithmetic errors with calculation of insulin doses.

Data from pumps can also be downloaded for personal records and/or shared with clinical teams. Increasingly, this can be performed remotely, but this carries its own challenges for healthcare providers and patients, with a danger of ‘data overload’. To aid with this, some professional CSII software can now also analyse patterns from downloaded data from CSII and/or continuous glucose monitoring (CGM).

Drawbacks of continuous subcutaneous insulin infusion

Drawbacks of CSII are:

- the risk of a more rapid deterioration in health if insulin delivery is interrupted because of the absence of long-acting background insulin, meaning insulinopenia and ketosis can develop more rapidly
- being connected constantly to a device (a new generation of small, aesthetically acceptable pumps may overcome this for some patients)
- even with increasingly automated systems (see below), a high level of engagement and effort for patients to harness pumps safely, let alone effectively.

The higher cost of CSII compared with injections means that, in many countries, CSII is reserved for a subset of patients who have struggled to achieve appropriate control of their diabetes (e.g. with continuing hypoglycaemia and/or hyperglycaemia) or where rapid control is desired (e.g. pregnancy, young children). In the UK, current National Institute for Health and Care Excellence (NICE) guidance is that, in adults, CSII should be considered in those with T1DM only where optimized therapy with injections has ‘failed’; this means $HbA_{1c} > 69$ mmol/mol ($> 8.5\%$) and/or hypoglycaemia being a significant problem.⁴

Continuous and ‘flash’ glucose monitoring

Most CGM systems consist of a self-inserted subcutaneous sensor linked wirelessly to a device acting as a receiver. The latter can be either the patient’s mobile phone (running on an app), a smartwatch or a specific stand-alone handheld device, or can be linked to an insulin pump that acts not just as a pump but also as the receiver for glucose information. Devices can display real-time information about both absolute blood glucose values and the direction and speed of change.

The system can be set to alert the patient if values are outside target ranges or, with predictive algorithms, to sound an alarm if glucose values are changing rapidly and/or predicted to move outside the target range.

Most devices ‘push’ information across to the receiving device. The FreeStyle Libre system (Abbott Diabetes Care) has been termed ‘flash’ glucose monitoring as it requires the user to ‘swipe’ a receiver or mobile phone over the sensor to view glucose information. The Eversense® system consists of a sensor inserted by a clinician under local anaesthesia in the upper arm with a transmitter applied externally over the arm and linked to a mobile phone app. The sensor lasts for up to 6 months but requires removal (also under local anaesthetic) after that time.

All such sensors detect changes in interstitial tissue glucose and then extrapolate back to actual blood glucose values. Most need regular capillary blood glucose measures for calibration, which can cause inaccurate interstitial glucose readings if calibration is not performed regularly.

Linking pumps with continuous glucose monitoring

An obvious pathway forward for this technology is to link real-time CGM information to control insulin delivery by CSII – described as closed-loop systems or more broadly as automated insulin delivery. There has been a gradual hierarchy of sophistication of these devices. The first approved automated feature was a low-glucose suspend option, with insulin delivery from a pump ceasing if CGM-measured glucose fell below a set point and patients failed to react to alarms. This evolved to include algorithms that predict hypoglycaemia in advance and alert and suspend insulin delivery before hypoglycaemia. The first ‘hybrid’ closed-loop system (automated insulin delivery combined with a manual bolus for meals) has now been commercialized. A number of other hybrid and fully closed-loop systems are in clinical trials and likely to be commercialized soon. There is also continued interest in developing dual-hormone closed-loop systems with a combination of insulin and another hormone such as glucagon or pramlintide (see below).

Transplantation

Whole-organ pancreas transplantation has a reasonable success rate for graft survival and insulin independence. In the UK, as in many countries, this is largely combined with kidney transplantation. However, transplantation of the pancreas alone can be performed where indicated – usually for recalcitrant severe hypoglycaemia. Similarly, islet transplantation involves a lesser procedural complexity but, like whole-organ transplantation, the risks of anti-rejection therapy including immunosuppression must be weighed against the benefits.

Non-insulin therapy to manage glucose levels in T1DM

As with type 2 diabetes, metformin can be used as an insulin sensitizer in T1DM, although a recent large clinical trial suggested that the effects may be modest. There is current interest in examining other drugs used to treat type 2 diabetes, such as pramlintide (slows gastric emptying), glucagon-like peptide-1 (GLP-1) agents, sodium glucose co-transporter (SGLT) inhibitors and others in T1DM, but all of these are currently unlicensed in

the UK and need further testing. SGLT-1 increases glucose transport into the body from the gastrointestinal tract, and SGLT-2 acts to reabsorb filtered glucose in the kidney. A number of clinical studies suggest that either SGLT-2 or combined SGLT1/SGLT2 inhibition improves glycaemic control in T1DM, and agents in this class may become licensed in near future as adjuvant therapy. Glucagon emergency pens are prescribable and, administered by a third party, are useful for treating severe hypoglycaemia. ◆

KEY REFERENCES

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TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online [here](#).

Question 1

A 25-year-old woman presented with poorly controlled diabetes mellitus. She had a 10-year history of type 1 diabetes. She was taking 40 U of a background insulin (glargine) in the morning and 20 U of a rapid-acting insulin (NovoRapid) with each meal. Investigation

- HbA_{1c} 108 mmol/mol (20–42); 12% (4.0–6.0)

Which of the following is the most appropriate initial management?

- Recommend a low-carbohydrate diet
- Start insulin pump therapy
- Arrange a refresher of self-management skills
- Change her insulin prescription
- Start her on a continuous glucose sensor

Question 2

A 45-year-old man presented acutely to the emergency department with hypoglycaemia. He had a 40-year history of type 1 diabetes. He was a delivery driver. After recovery, he said he had undergone Dose Adjustment for Normal Eating (DAFNE) training 5 years previously and that he attributed the episode to miscalculating the carbohydrates in his lunch. He had had a similar event 8 weeks previously at home, when his partner found him unconscious and treated him with buccal administration of glucose gel. He was now feeling fine and wanted to go home.

What is best option for managing him now?

- Admit to hospital for diabetes team review
- Discharge with no change in management
- Discharge with early review in primary care suggested
- Discharge but recommend referral for islet transplantation
- Discharge with secondary care follow-up

Question 3

A 45-year-old woman presented to the emergency department in the morning having woken up feeling unwell and dehydrated. She had type 1 diabetes and had been using insulin pump therapy for the previous 6 months. She said that her glucose control had been much better on the pump, and she attributed the current events to having changed an infusion set/cannula immediately before going to sleep the previous night. She was a visitor to the area.

Investigations

- Blood pH 7.39 (7.35–7.45)
- Plasma glucose 18 mmol/litre (3.0–6.0)
- Plasma β -hydroxybutyrate 1.5 mmol/litre (0.4–0.5)

What is the best management?

- Admit her to hospital and manage her using the usual diabetic ketoacidosis protocol
- Admit her to hospital and start a 'sliding scale' variable rate intravenous insulin infusion
- Advise bolus insulin subcutaneously, change the infusion set and discharge her if well after 2 hours
- Admit her but keep her on the pump with additional intravenous fluids
- Discharge with antibiotics and recommend an early review by own diabetes team