Clinical DIGEST 1

Management of type 1 diabetes



The ability to achieve an optimal HbA_{1c} is determined by the clinic, not the individual

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¶ he study by Kuhtreiber et al, summarised alongside, looked at the relationship between residual insulin secretion and long-term blood glucose control and diabetic complications. Many studies have previously demonstrated that residual insulin secretion is associated with better glycaemic control, fewer hypoglycaemic episodes and fewer complications. Kuhtreiber et al used measurement of small amounts of residual insulin secretion via an ultra-sensitive C-peptide assay to identify and stratify people with type 1 diabetes who are at risk of or have protection from complications and hypoglycaemia. They found the earlier the onset of diabetes, the faster the decline in insulin secretion, which fits with the clinical observation that people with long-standing diabetes often have very "brittle" diabetes where recurrent severe hypoglycaemia occurs, despite a high HbA₁₀. So does it matter? The answer is a clear yes and one that I have referred to in previous commentaries.

Early tight control preserves residual insulin secretion (Madsbad et al, 1981), and the HbA_{1c} achieved during the first year after diagnosis is predictive of longer-term control (Scott et al,

2006). The ability to achieve a normal HbA_{1c} after diagnosis is determined by the centre or clinic, not the patient with diabetes. This was clearly demonstrated in 1999 when Peter Swift from Leicester looked at the percentage of patients achieving this goal during the first year after diagnosis among a number of paediatric and adolescent diabetes units in the Trent region in the UK (Swift et al, 1999). The range among the clinics was 0% to nearly 70%. The long-term outcomes of patients are within the gift of healthcare professionals. We must set ourselves clear targets and provide support services that allow recently diagnosed people with diabetes to achieve high degrees of self-management.

Madsbad S, Krarup T, Regeur L et al (1981) Effect of strict blood glucose control on residual beta-cell function in insulin-dependent diabetics. *Diabetologia* **20**: 230–4

Scott AR, Bouchier D, Bruce R et al (2006) First National Audit of the outcomes of care in young people with diabetes in New Zealand – high prevalence of nephropathy in Maori and Pacific Islanders. NZ Med J119: U2015

Swift PG (1999) Utilising the partial remission phase for a multicentre audit of glycaemic control in the first year after diagnosis. *Diab Res Clin Pract* **44**: (Suppl) S32P62

Diabet Med

Residual insulin production: Protective effect?

Readability ////
Applicability to practice ////
WOW! Factor ////

C-peptide monitoring is a way of measuring insulin production, and although production decreases after onset of T1D, the reduction can be slow. Based on evidence from C-peptide assays, studies suggest that beta-cells are frequently viable and function decades after T1D diagnosis.

Ultra-sensitive assays now enable detection of C-peptide levels as low as 1.5–2.5 pmol/L compared to regular assays which can detect to approximately 50 pmol/L.

The authors evaluated C-peptide levels, duration of disease and age of onset in over 1000 people with T1D to make associations with rates of complications.

In this cohort, C-peptide levels declined for decades after diagnosis and the rate of decline was significantly related to the age of onset (*P*<0.0001), adjusting for disease duration.

5 C-peptide levels >10 pmol/L were found to be protective of complications (e.g. nephropathy, neuropathy, foot ulcers and retinopathy [*P*=0.03]).

Low C-peptides were associated with poor metabolic control measured by HbA_{rc} (*P*<0.0001).

The lowest C-peptides levels were associated with mild (P=0.049) or moderate (P=0.04) hypoglycaemia.

C-peptide levels are helpful in characterising groups of people who are at risk of complications, faster decline C-peptide, poorer metabolic control and severe hypoglycaemia.

Kuhtreiber WM, Washer SL, Hsu E et al (2015) Low levels of C-peptide have clinical significance for established type 1 diabetes. *Diabet Med* **32**: 1346–53

Diabetes

Diazoxide: A treatment for hypoglycaemia?

Readability	////
Applicability to practice	JJJJ
WOW! Factor	JJJJJ

Diazoxide is involved in the hormonal regulation of glucose. It is a potassium channel activator and is used in the USA as a treatment of hypoglycaemia in situations such as inoperable islet cell adenoma, as it inhibits the secretion of insulin from the pancreas

People with T1D are at risk of severe hypoglycaemia from insulin treatment and it is believed that ATP-sensitive potassium channels may be involved in the detection of hypoglycaemia.

Twelve adults with T1D completed the double-blind, placebo-controlled, randomised controlled trial. Participants received both diazoxide and placebo orally on two separate days, separated by more than 2 weeks, and underwent a hyperinsulinaemic—hypoglycaemic clamp study. Continuous glucose monitoring was used for 48 hours prior to the clamp study to ensure there were no hypoglycaemia events before the intervention.

Diazoxide resulted in a 37% increase in plasma levels of adrenaline and a 44% increase in plasma noradrenaline during hypoglycaemia compared with placebo.

- The authors showed that diazoxide (7 mg/kg) given before acute hypoglycaemia can significantly increase the magnitude of adrenaline and noradrenaline counter-regulatory responses.
- Longer-term treatment of diazoxide could improve hypoglycaemia awareness and reduce the frequency of severe hypoglycaemia.

George PS, Tavendale R, Palmer CN, McCrimmon RJ (2015) Diazoxide improves hormonal counterregulatory responses to acute hypoglycemia in long-standing type 1 diabetes. *Diabetes* **64**: 2234–41

Diabetologia

Islet transplantation among the socioeconomically deprived population

Readability	////
Applicability to practice	<i>////</i>
WOW! Factor	////

- Islet transplantation can be useful for people with hypoglycaemia unawareness, and nationally funded programmes have been implemented to identify the people who would benefit most from the procedure. This study aimed to determine whether the socioeconomically deprived population with T1D is being reached with islet transplantation as hypoglycaemia is a common complication in this group.
- In total, 106 people were referred and 18 people received islet transplants in a single UK centre in Scotland. They completed pretransplantation tests and were followed for ≥12 months after transplantation.
- Among those referred and those who received transplantation, there was a greater prevalence of people who were socioeconomically deprived compared to the general population (*P*<0.05).
- Three-quarters of the cohort were socioeconomically deprived, 88% did not hold a driver's licence and nearly all had a reduced ability to work (all *P*<0.05).
- After 12 months, 93% had improved hypoglycaemia awareness and glycaemic control, diminished glycaemic lability and decreased central adiposity (all *P*<0.05).
- lslet transplantation programmes can and do reach the socioeconomically deprived and can result in improvements in clinical features and quality of life.

Forbes S, McGowan NW, Duncan K et al (2015) Islet transplantation from a nationally funded UK centre reaches socially deprived groups and improves metabolic outcomes. *Diabetologia* **58**: 130–8

Diabetes Care

Online teleconferencing for children with T1D and their caregiver

Readability	////
Applicability to practice	////
WOW! Factor	JJJJ

This study aimed to compare the relative effectiveness of two modes of delivering Behavioural Family Systems Therapy for Diabetes (BFST-D) to improve adherence and glycaemic control for children with T1D and their family or carers.

The modes under investigation in this US clinic were face-to-face in the clinic and video conferencing using Skype.

Ninety adolescents with suboptimal glycaemic control were randomised equally to receive either mode of therapy with at least one adult caregiver. The therapy consisted of 10 sessions over a 12-week period.

Mean age of participants was 15.04 years and 55% were male. Measures of adherence and glycaemic control were taken before and after the intervention at a follow-up appointment 3 months later.

No significant between-group differences were identified before or after the intervention or in the follow-up assessment, but there were statistically significant improvements in adherence and glycaemic control after the intervention compared to before. Improvements were maintained at 3-month follow-up.

The authors concluded that delivering care via teleconferencing is a viable and effective alternative to face-to-face clinic appointments, especially for children who are non-adherent to appointments and who have suboptimal control.

Harris MA, Freeman KA, Duke DC (2015) Seeing Is Believing: Using Skype to improve diabetes outcomes in youth. *Diabetes Care* **38**: 1427–34

transplantation programmes can, and do, reach the socioeconomically deprived and can result in improvements in clinical features and quality of life.