Management of type 1 diabetes

Cystic fibrosis-related diabetes: A growing problem needing careful clinical management

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

Adults with cystic fibrosis (CF) are increasingly common (Buzzetti et al, 2009) and management of their diabetes can be challenging. In this excellent article (Laguna et al, 2010; summarised alongside), the pathophysiology is described and the differences between CF-related diabetes (CFRD) and types 1 and 2 diabetes are explained. I must confess that I was unaware that there are different CF mutations of differing severity, and that different diabetes prevalence (for reasons that are not clear) are associated with the different mutations.

Not all young people with CF develop diabetes, despite having exocrine pancreas destruction to one degree or another. Because of residual insulin secretion, diabetic ketoacidosis is rare in CFRD and, should it occur, is suggestive of coexistent type 1 diabetes. In these circumstances, it is worth measuring autoantibodies.

In addition, not all glucose intolerance in the person with CF is diabetes. CFRD diagnosis is based on the results of an oral glucose tolerance test and the authors discourage the use of an HbA_{1c} level ≥6.5% (≥48 mmol/mol) for diagnosing diabetes as many people with CF have an abnormal oral glucose tolerance test with an HbA_{1c} level of less than this. Screening for CFRD is recommended from 10 years of age.

For any healthcare professional used to treating disaffected young people with type 1 diabetes who frequently run blood glucose levels in the teens, it comes as something of a shock when asked to initiate insulin in a young person with CF who only has postprandial hyperglycaemia. Nevertheless, insulin therapy has been associated with weight gain and improved nutritional status in CF – a key factor in improved survival.

People with CFRD have worse pulmonary function than those without diabetes and are more prone to certain infections. Laguna et al place much emphasis on the different types of glucose intolerance seen in these young adults with CF, but only passing mention is made of the difficulty of achieving good glycaemic control in those with established CFRD. Infections, steroids and overnight enteral feeding makes selecting the best insulin regimen challenging. Some centres use continuous subcutaneous insulin infusion, but there are few published studies of their efficacy in comparison with multiple daily injection regimens.

> ***"Cystic fibrosis-related diabetes is an oft overlooked area of diabetes care, and an area in which many diabetes centres have little experience."***

CFRD is an oft overlooked area of diabetes care, and an area in which many diabetes centres have little experience. Laguna et al's article is well worth reading.

Buzzetti R, Salvatore D, Baldo E et al (2009) An overview of international literature from cystic fibrosis registries: 1. Mortality and survival studies in cystic fibrosis. *J Cyst Fibros* **8**: 229–37

DIABETES, OBESITY AND METABOLISM

Managing diabetes in cystic fibrosis

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

1 Cystic fibrosis-related diabetes (CFRD) is the most common comorbidity of cystic fibrosis (CF) and is associated with worsening clinical status and increase mortality.

2 Approximately 20% of adolescents with CF have CFRD, with the main disease burden falling on adults with CF (40–50%).

3 CFRD aetiology is distinct from both types 1 and 2 diabetes, being characterised by a combination of insulin resistance, insulin deficiency and a genetic predisposition to diabetes.

4 It has been established that people homozygous for Class IV CFRD are less likely to develop diabetes than those with more severe mutations.

5 Those with CFRD have more severe pulmonary disease, more pulmonary exacerbations and a higher prevalence of traditional CF sputum pathogens than those with CF but no diabetes.

6 The increased life-expectancy of people with CFRD will likely lead to an increased burden of microvascular disease in this population; screening for retinopathy, nephropathy and peripheral neuropathy should commence 5 years after a CFRD diagnosis.

7 HbA_{1c} levels are lower in CF populations, thus a diagnosis of CFRD should not be ruled out in those with an HbA_{1c} level <6.5% (<48 mmol/mol), rather an oral glucose tolerance test (≥11.1 mmol/L) should be used.

8 Target HbA_{1c} levels for people with CFRD have not been firmly established. The authors recommend frequent testing of the person with CFRD as an HbA_{1c} trend may be a useful indicator of improving or worsening glycaemic control.

Laguna TA, Nathan BM, Moran A (2010) Managing diabetes in cystic fibrosis. *Diabetes Obes Metab* **12**: 858–64

DIABETES TECHNOLOGY & THERAPEUTICS

Insulin pump therapy improves HbA_{1c} levels in girls with T1D and eating disorders

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

1 The feasibility of insulin pump therapy (IPT) to treat T1D in adolescent girls (n=63; aged >10 years) with eating disorders (EDs) was investigated.

2 Fifteen girls with EDs (eight received IPT; seven received multiple daily injections [MDI]) and 48 girls without EDs were treated with IPT.

3 Mean HbA_{1c} in the ED-IPT group was significantly lower than in the ED-MDI group (9.07±1.33% vs 10.40±2.01% [76 vs 90 mmol/mol]; P=0.04) by study end. The authors concluded that IPT was more effective in improving HbA_{1c} in this cohort with EDs.

Pinhas-Hamiel O, Graph-Barel C, Boyko V et al (2010) Long-term insulin pump treatment in girls with type 1 diabetes and eating disorders – is it feasible? *Diabetes Technol Ther* **12**: 873–8

DIABETES & METABOLISM

CSII reduces hypos in those at risk

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

1 People (n=13) with T1D using continuous subcutaneous insulin infusion (CSII) with more than six recorded capillary blood glucose values <60 mg/dL (3.3 mmol/L) in the past 14 days used a continuous glucose monitoring (CGM) device for 12 weeks, followed by a 12-week crossover period of self-monitoring of blood glucose only, or vice versa.

2 A significant decrease in HbA_{1c} from 8.3±0.7 to 7.7±0.6% (67 to 61 mmol/mol) among those using CGM was observed (P=0.049).

3 Among the nine study completers, the number of low CBG values while using CGM decreased from 13.9±9.2 to 7.6±6.8 (P=0.011).

Radermecker RP, Saint Remy A, Scheen AJ et al (2010) Continuous glucose monitoring reduces both hypoglycaemia and HbA_{1c} in hypoglycaemia-prone type 1 diabetic patients treated with a portable pump. *Diabetes Metab* **36**: 409–13

DIABETOLOGIA

T1D survival on par with general population if renal disease excluded

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

1 Data from a large USA study were examined for cause of death among people with T1D, stratified by renal status.

2 During a median 20-year follow-up, standardised mortality ratios for overt nephropathy (>200 µg/min) and end-stage renal disease (dialysis, renal transplantation) were 12.5 (9.5–15.4) and 29.8 (16.8–42.9), respectively.

3 Excluding those with renal disease, no significant excess mortality was observed in those with T1D when compared with the general population. Progression to renal disease was found to significantly increase mortality in T1D.

Orchard TJ, Secrest AM, Miller RG, Costacou T (2010) In the absence of renal disease, 20 year mortality risk in type 1 diabetes is comparable to that of the general population: a report from the Pittsburgh Epidemiology of Diabetes Complications Study. *Diabetologia* **53**: 2312–9

"Excluding those with renal disease, no significant excess mortality was observed in those with T1D when compared with the general population. Progression to renal disease was found to significantly increase mortality in T1D."