CYSTIC FIBROSIS RELATED DIABETES

Sarah Collins
CF Specialist Dietitian Royal Brompton & Harefield NHS Foundation Trust

Cystic fibrosis related diabetes (CFRD) affects 40-50% of adults with cystic fibrosis.[1] Its presence has a significant impact on nutritional status, lung function, morbidity and mortality.

Cystic fibrosis (CF) is the most common life-threatening inherited disease in the Caucasian population, affecting 10,583 people in the UK. It is a progressive, multisystem disease affecting vital organs of the body, especially the lungs and digestive system. It is usually diagnosed soon after birth, although symptoms occur throughout life. In the 1930s, when CF was first described, 70% of babies with CF died within the first year of life; today the median age of survival is a 40.1 years.[2,3] Improvement in survival has led to the development of more complications, with diabetes being the most common co-morbidity of CF.

PREVALENCE

In the UK, 27.6% of the CF population (1924 people) have cystic fibrosis related diabetes (CFRD).[3] The prevalence of CFRD increases with age; with 2.0% children, 19% adolescents and 40-50% of adults having CFRD.[1]

Sarah works as a Specialist Dietitian with adults who have cystic fibrosis and has done for the past 19 years. She has a particular interest in the management of CF related diabetes.

PATHOPHYSIOLOGY

Whilst CFRD shares features of Type 1 and Type 2 diabetes, it is a distinct clinical entity (Table 1). Its pathophysiology is not fully understood, however, the primary defect in CFRD is insulin deficiency. Destruction of the pancreatic tissue, with accompanying fibrosis and disorganisation of the islet cells gradually results in a reduction in insulin production. Insulin resistance can also contribute to the development of CFRD and it is variable over time due to changes in clinical status. Factors that contribute to increased insulin resistance include: acute respiratory exacerbations, chronic severe lung disease and glucocorticoid therapy[4]. The presence of CF liver disease may also affect glucose handling in people with CF.

CLINICAL SIGNIFICANCE

The early stages of insulin deficiency contribute to morbidity and mortality due to a catabolic decline in weight and respiratory muscle function, as well as the promotion of bacterial growth by the presence of hyperglycaemia.[5] A decline in clinical status and lung function has been observed several years before CFRD is diagnosed.[6-8] Improvement in

Table 1: Comparison between CFRD, Type1and Type 2 diabetes

	Type 1	Type 2	CFRD
Average age of onset	<40 years	>40 years	18-21 years
Typical BMI	average	high	low
Insulin resistance	minimal	significant	variable
Insulin secretion	absent	variable	decreased
Ketosis	common	rare	very rare
Microvascular complication	yes	yes	Yes
Macrovascular complications	yes	yes	uncertain

Cystic fibrosis related diabetes is part of a continuum of abnormalities in glucose tolerance, with only a few people with CF having completely normal glucose tolerance.

weight has been seen prior to the development of overt CFRD with the early initiation of insulin.[9-12] The presence of CFRD is linked to worse lung function in people with CF regardless of age. Targeting CF specific outcomes such as BMI and lung function provides evidence for supporting early treatment of CFRD, particularly before advanced lung disease occurs.

The risk of death has also been shown to be higher in patients with CFRD - three times greater in those with HbA1c >6.5% (48mmol/mol), indicating that glycaemic control may also be a contributory factor.[13] Optimising glycaemic control results in improvements in nutritional status and lung function, reduces mortality[14] and the development of long-term microvascular complications.[15,16]

SCREENING

Early detection of abnormalities of glucose levels is important to prevent weight loss and decline in lung function. Cystic fibrosis related diabetes is part of a continuum of abnormalities in glucose tolerance, with only a few people with CF having completely normal glucose tolerance. In early stages of glucose intolerance the diagnosis of CFRD is difficult to make with the majority of people not presenting with overt clinical symptoms. The initial abnormality seen in CFRD is a delayed first-phase insulin response with the preservation of basal insulin.

It is recommended that CFRD should be diagnosed based on response to a standard 75g oral glucose tolerance test (OGTT), and that screening should be done annually in all people with CF greater than 10 years.[17] There is, however, several problems with this test in people with CF. Firstly, fasting glycaemia is often normal in the early stages of CFRD and secondly, glucose levels can vary widely due to patterns of insulin secretion in CF and values can fall to normal by 120 minutes. The cut off is based on criteria for reducing cardiovascular complications in treatment of Type 2 diabetes. In CFRD, we are treating hyperglycaemia with insulin for the clinical benefit. Serial blood glucose monitoring and/or continuous glucose monitoring systems (CGMS) are, therefore, essential when assessing the need for treatment.

Women with CF are at increased risk of developing gestational diabetes and screening using the OGTT should take place in the preconception period.[17,18] It should be repeated between 12-16 weeks and 24-28 weeks gestation and if random blood glucose levels are elevated.[17]

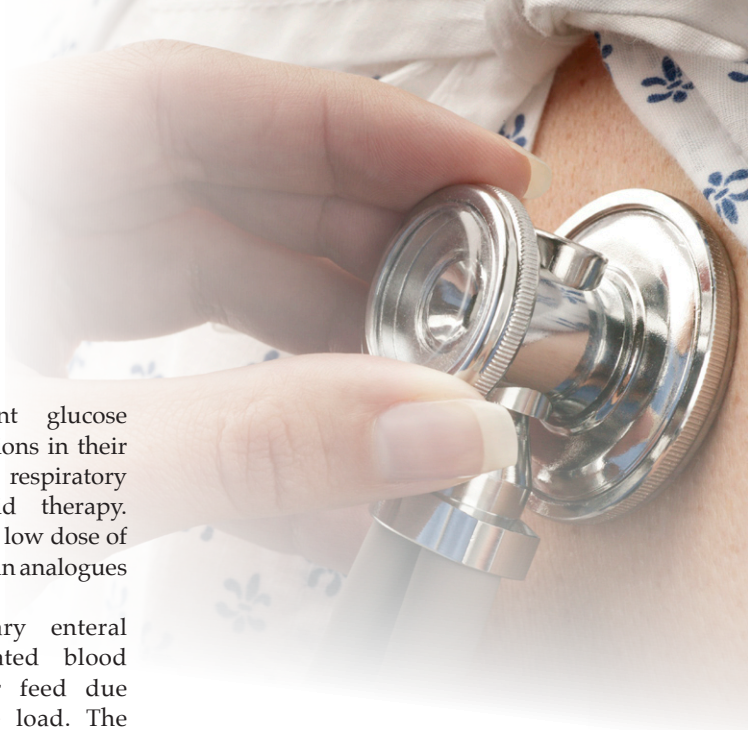
TREATMENT

Insulin is the recommended treatment of choice for people with CFRD as insulin deficiency is the primary cause of CFRD. The aims of management of CFRD are to maintain optimal growth, nutritional status and lung function, to achieve good control of blood glucose levels and to avoid long-term microvascular complications.[18]

Varying insulin regimens are used, they should be tailored according to individual requirements, taking into account clinical and nutritional status, appetite and level of physical activity. In our centre, we tend to give insulin in the following situations:

- In those patients who have been found to have minor abnormalities in their glucose metabolism (identified through OGTT, serial blood glucose monitoring and in some cases CGMS) and who have poor nutritional and clinical status. Insulin will be initiated for its anabolic enhancing properties; this will usually be on a low dose of basal insulin taken once daily.

Achieving and maintaining a good nutritional status is an essential part of survival in CF



- In patients with intermittent glucose tolerance who only show elevations in their blood glucose levels during respiratory exacerbations or glucocorticoid therapy. These patients will be on either a low dose of basal insulin or quick acting insulin analogues with some but not all meals.
- In patients on supplementary enteral feeds who experience elevated blood glucose when receiving their feed due to the increased carbohydrate load. The insulin prescribed will be dependent on the duration and type of the supplementary feed used.
- In those patients who have post-prandial rises in blood glucose quick acting insulin analogues will be given with food (initially this may not be with all meals). Many patients do not need basal insulin initially or indeed for many years in some cases. Eventually they will progress to requiring a basal bolus insulin regimen.

A collaborative multidisciplinary approach between CF specialists and a diabetes team that is familiar with CFRD and its unique features is advised.[17,18] People with CFRD need education and support tailored to their nutritional requirements, insulin regimen and clinical status.

The number of people with CF requiring insulin will increase because the CF population is growing and ageing and survival rates are improving. Currently 59.3% of the UK CF population is 16 years and over.[3] Cystic fibrosis teams are very aware of the consequences of hyperglycaemia and insulin is initiated much earlier, before overt hyperglycaemia occurs, to reduce morbidity and mortality.

CHALLENGES IN THE MANAGEMENT OF CFRD

The diagnosis and onset of diabetes in people with CF signifies the development of a second chronic illness, with it comes its own burden of treatment and monitoring in addition to the meticulous daily treatments associated with the management of CF. People with CF have a high treatment burden with increased complexity in treatments seen in adulthood; this in itself poses challenges for self-management and concordance[19]. People with CFRD are not a homogenous population; their therapeutic needs are diverse, challenging and continually evolving.

NUTRITIONAL MANAGEMENT

Achieving and maintaining a good nutritional status is an essential part of survival in CF; there is a strong link between lung function and nutritional status. Regular dietetic input is a critical component of CF care so that any nutritional decline can be minimised and dietetic intervention can be adjusted to meet changes in physical, clinical and psychosocial needs. The majority of people with CF can achieve good nutritional status by following a high-energy diet however a minority may need oral nutritional supplements or artificial nutritional support. Management must be individualised as the nutritional needs of people with CF vary greatly.

Table 2: Dietary recommendations for people with CFRD

	Underweight (BMI <20kg/m2)	Healthy weight (BMI 20-25kg/m2)	Overweight (BMI >25kg/m2
Dietary aim	Improve nutritional status	Maintain nutritional status	Prevent further weight gain or promote weight loss
Dietary restrictions	Minimise	Some	Some/moderate
Carbohydrates	Modify timing of simple carbohydrate	Restrict simple carbohydrates to meal times	Restrict simple carbohydrates
Fibre	May limit	Moderate	Encourage
Fat	Encourage (PUFA/MUFA)	As required (PUFA/MUFA)	Modify intake (PUFA/MUFA)
Salt	As required	As required	Monitor - particularly in people on anti-hypertensive therapy

People with CFRD are advised that dietary guidelines of modified energy, low-protein, low-fat and low-salt intakes, as recommended for people with Type 1 and Type 2 diabetes, are not always appropriate.[18,20]

A detailed dietary review should be conducted by a CF specialist dietitian and advice given on a diet appropriate to meet individual nutritional requirements taking into account clinical and nutritional status, appetite and physical activity (Table 2). Often, people with CF can have erratic dietary intakes and some have a heavy reliance on foods high in simple carbohydrates such as jelly-type sweets and sugary energy drinks, making management of CFRD challenging. Advice given on carbohydrate intakes will be based upon nutritional status and requirements, with the majority being advised to have regular meals containing complex carbohydrates and to modify the quantity and timing of simple carbohydrates. People with CFRD are taught carbohydrate awareness with some being taught how to carbohydrate count and adjust their insulin doses according to their carbohydrate intake. This is particularly useful if they have very variable and erratic eating habits.

To maintain or improve nutritional status, some people with CF will need to take oral nutritional supplements on a routine basis. The majority of oral nutritional supplements contain carbohydrates and, therefore, insulin will be required. The type and amount of insulin required will vary according to the supplement used, when it is taken and the volume consumed.

For those people with CF who receive supplementary enteral tube feeds their insulin regimens will need to be modified to optimise glycaemic control, taking into account the composition, volume and duration of the feed.

A diet high in fat and energy has been part of the nutritional management of CF for the past 35 years and, recently, the over-reliance on saturated fat in the diet has been highlighted.[21] With the improvements in survival seen in people with CF, this is of concern and a diet more cardio-protective may therefore be of benefit. The use of mono- and polyunsaturated fats is, therefore, encouraged in all people with CF. Overweight and obesity are also becoming increasingly common problems in CF.[22,23] Nutritional advice should, therefore, be individualised to meet changes in nutritional requirements and dietary modifications may be required to support long-term health and well-being.

CONCLUSIONS

Cystic fibrosis related diabetes is a common complication of CF affecting 40-50% of adults; its presence has a significant impact on nutritional status, lung function and survival. People with CFRD should be treated at specialist CF centre by a multidisciplinary team with expert knowledge of the management of CFRD. They should receive individualised dietary advice and be given appropriate insulin regimens in order to gain optimal control of their CFRD and prevent the risk of long-term microvascular complications.

For article references please email:
info@networkhealthgroup.co.uk