

Cystic Fibrosis–Related Diabetes on the Increase

BY BRUCE JANCIN
Denver Bureau

KEYSTONE, COLO. — The prevalence of cystic fibrosis–related diabetes is skyrocketing in parallel with the rising average life span of the cystic fibrosis population, Dr. Robert Slover said at a conference on the management of diabetes in youth.

Cystic fibrosis–related diabetes (CFRD) is a unique endocrine disorder that's neither type 1 nor type 2 diabetes. Its treatment differs in important ways from familiar diabetes-management strategies.

CFRD is the most common comorbid complication of CF. The prevalence of CFRD in the United States jumped from 4.4% in 1992 to 12% in 2002, a 173% rise in just a decade. The prevalence increases with age such that CFRD affects 14% of CF patients aged 13 years and older and at least 25% of those aged 35–44 years. Some studies estimate the prevalence of CFRD after age 30 at up to 43%, noted Dr. Slover, a pediatrician at the Barbara Davis Center for Childhood Diabetes at the University of Colorado, Denver.

The peak age of onset of CFRD is 18–23 years—older than for type 1 and younger than for type 2 diabetes. Unlike in type 1 diabetes, insulin deficiency in CFRD is not due to autoimmunity; autoantibodies are absent, as in type 2 disease. Instead, the insulin deficiency of CFRD results from fibrotic scarring and destruction of pancreatic islets and beta cells.

As in type 2 diabetes, ketoacidosis is rare in CFRD. All three forms of diabetes are associated with the microvascular complications of retinopathy, nephropathy, and gastroparesis. To date, an increase in macrovascular complications hasn't been reported with CFRD, although most experts believe it will with longer follow-up, Dr. Slover said at the conference, sponsored by the university and the Children's Diabetes Foundation at Denver.

Data from the CF Foundation patient registry indicate mortality is sixfold greater among CF patients with CFRD than in those without it. Sixty percent of CF patients without diabetes survive to age 30 years, compared with 25% with CFRD.

For unknown reasons, this excess mortality is concentrated in females. A retrospective study of 1,081 CF patients fol-

lowed at the University of Minnesota, Minneapolis, over a 25-year period showed median survival among females with CF but not diabetes was 47.0 years, compared with 30.7 years for females with CFRD. In contrast, CFRD in males was associated with a mere 2-year decrease in survival.

Other studies have shown that females with CFRD have a 20% reduction in forced expiratory volume in 1 second, while males don't. Genetics also figure into the picture; the delta 508 homozygous geno-

type confers near-universal pancreatic insufficiency and an increased risk of CFRD.

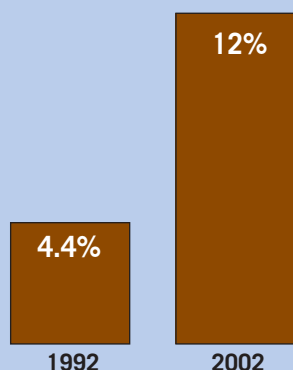
Poorly controlled CFRD is associated with a striking worsening of CF clinical status, including more pulmonary exacerbations requiring parenteral antibiotics, high-viscosity sputum, and a greater prevalence of clinically important sputum pathogens.

A Danish population study suggests the prediabetic state leads to marked worsening of CF rather than the converse, that

more severe CF predisposes to diabetes. In the Danish cohort, weight loss and deteriorating pulmonary function began 4–6 years before diabetes onset. After 2 years on insulin, patients' weight returned to their levels of 6 years earlier and pulmonary function stabilized. The current hypothesis, Dr. Slover said, is that insulin deficiency in CF results in protein and fat catabolism even in the presence of relatively normal blood glucose levels, with negative impact on morbidity and mortality. ■



Prevalence of Diabetes in Cystic Fibrosis Patients Has Risen 173%



Source: Dr. Slover

ELSEVIER GLOBAL MEDICAL NEWS

Important Safety Information:

- Antidepressants increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders.
- Patients started on therapy should be observed closely for clinical worsening, suicidality, or unusual changes in behavior.
- Cymbalta is not approved for use in pediatric patients.

Cymbalta should not be used concomitantly with monoamine oxidase inhibitors (MAOIs) or thioridazine and not in patients with a known hypersensitivity or with uncontrolled narrow-angle glaucoma.

Clinical worsening and suicide risk: All adult and pediatric patients being treated with an antidepressant for any indication should be observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially when initiating drug therapy and when increasing or decreasing the dose. A health professional should be immediately notified if the depression is persistently worse or there are symptoms that

Reference: 1. Data on file, Lilly Research Laboratories: CYM20050314A, B&D.

*Cymbalta vs placebo ($P \leq .001$) by MMRM on 24-hr average pain severity score
Cymbalta vs placebo ($P \leq .009$) by MMRM on 24-hr night pain severity score