OBSERVATIONS

Hypoglycemia in Adults With Cystic Fibrosis During Oral Glucose Tolerance Testing

Cystic fibrosis–related diabetes (CFRD) is the most common comorbidity in patients with cystic fibrosis (CF) (1). Consensus guidelines state that all patients above the age of 10 years should be screened annually for CFRD with a 2-h 75-g oral glucose tolerance test (OGTT) (2). There are four categories of glucose tolerance based on OGTT fasting and 75-g 2-h glucose levels: normal glucose tolerance, impaired glucose tolerance (IGT) with 2 h level 7.8–11.1 mmol/L, CFRD without fasting hyperglycemia (CFRD FH−) with 2-h level > 11.1 mmol/L, and CFRD with fasting hyperglycemia (CFRD FH+) (2).

At our institution in 2011, there were 167 pre–lung transplant adult CF patients, of whom 46 had preexisting CFRD. Of the remaining, 28 agreed to the test; 3 were found to have CFRD FH−, 1 was found to have CFRD FH+, and 1 had an incomplete test. Of the remaining 23, 7 had IGT.

For the 28 who agreed to testing, age, sex, and BMI were 27.2 ± 5.9 years of age, 61% male, and 22.2 ± 2.7 kg/m^2. For the 23 without CFRD, fasting and 1-, 2-, and 3-h glucose levels were 5.5 ± 0.9 mmol/L, 11.4 ± 3.5 mmol/L, 7.4 ± 3.3 mmol/L, and 3.4 ± 1.2 mmol/L, respectively (Fig. 1). At 2 h, one patient with symptomatic hypoglycemia at 2.4 mmol/L did not continue. At 3 h, 13 of the remaining 22 (59%) were found to have blood glucose levels <3.9 mmol/L, 10 (45%) had levels <3.3 mmol/L, 6 (27%) had levels <2.8 mmol/L, and 3 (14%) had levels <2.2 mmol/L.

The benefit of identification of CFRD and IGT in CF is supported by a small improvement in BMI (0.39 BMI units) in patients with CFRD FH− treated with insulin in a 1-year randomized multicenter study (3). Epidemiological studies have shown that higher BMI is an independent predictor of improved survival in CF.

Hyperglycemia in CF appears to be primarily due to β-cell failure over time (4). What is not as well understood are the dynamics of islet hormones in an adult CF population, particularly glucagon secretion with meals or hypoglycemia. In our patients, we saw frequent hypoglycemia 3 h after a 75-g oral glucose load and occasionally at the 2-h time point. While 3-h OGTT glucose levels have not been measured before, fasting hypoglycemia has been described in a pediatric and adult CF population (5).

Our patients were symptomatic, and although no one required assistance for treatment, glucose levels <2.2 mmol/L in patients represents islet pathology. While glucagon deficiency in the context of a delayed insulin response is an attractive possibility for etiology, further study is required to answer this question.

In conclusion, 3-h testing for CFRD in adults with an OGTT can result in 3-h hypoglycemia; patients should be cautioned regarding the symptoms of hypoglycemia after a 2-h test along with measures to treat those symptoms. The etiology and long-term significance of the CF abnormal glucose response warrants further study.

IRL B. HIRSCH, MD[1]
MARY M. JANCI, MSN[2]
CHRISTOPHER H. GOSS, MD, MSC[3]
MOIRA L. AITKEN, MD[3]

From the [1]Department of Medicine, Division of Metabolism, Endocrinology & Nutrition, University of Washington School of Medicine, Seattle, Washington; the [2]Diabetes Care Center, University of Washington Medical Center, University of Washington School of Nursing, Seattle, Washington; and the [3]Department of Medicine, Division of Pulmonary and Critical Medicine, University of Washington School of Medicine, Seattle, Washington.
Corresponding author: Irl B. Hirsch, ihirsch@uw.edu.

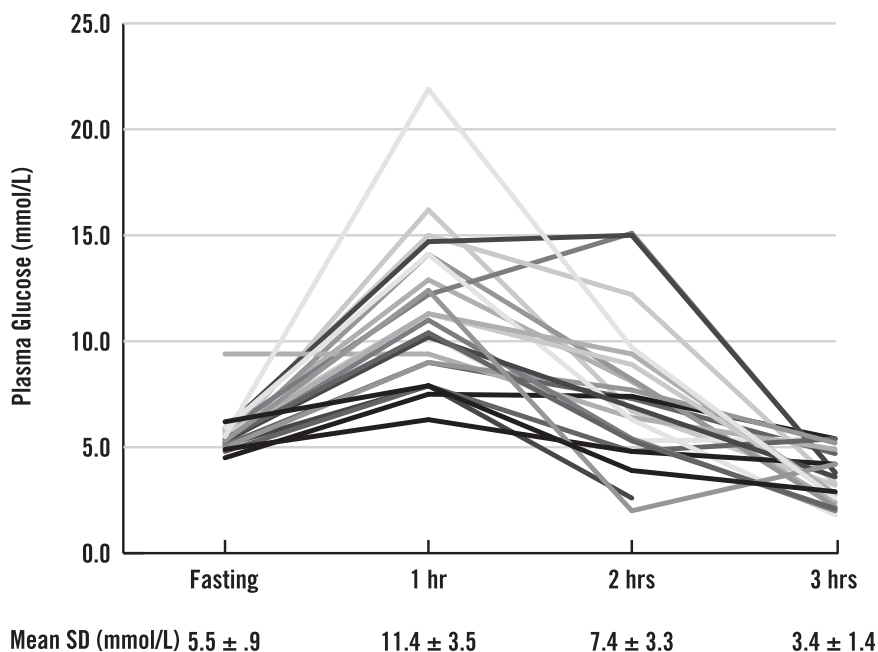| Mean SD (mmol/L)	5.5 ± .9	11.4 ± 3.5	7.4 ± 3.3	3.4 ± 1.4
	Fasting	1 hr	2 hrs	3 hrs

Figure 1—*Serum glucose of 23 CF patients undergoing an OGTT over a 3-h time period. There can be marked hypoglycemia at both the 2-h and 3-h time point. hr, hour.*

References

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