AN UPDATE ON CFRD AND OUR CENTER’S PROTOCOL:
KEEPING IT SHORT AND SWEET!

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Cystic Fibrosis Related Diabetes:

Type 1: lack of insulin secretion

Type 2: insulin resistance/decreased insulin secretion
CFRD Is a Distinct Form of Diabetes:

<table>
<thead>
<tr>
<th>Feature</th>
<th>Type 1</th>
<th>Type 2</th>
<th>CFRD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most common age of onset</td>
<td>&lt;20</td>
<td>&gt;40</td>
<td>22-24</td>
</tr>
<tr>
<td>Usual body habitus</td>
<td>Normal</td>
<td>Obese</td>
<td>Normal</td>
</tr>
<tr>
<td>Insulin Secretion</td>
<td>Absent</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Insulin Sensitivity</td>
<td>↓</td>
<td>↓↓↓↓</td>
<td>↓</td>
</tr>
<tr>
<td>Autoimmune etiology</td>
<td>Yes</td>
<td>No</td>
<td>↓</td>
</tr>
<tr>
<td>Ketoacidosis</td>
<td>Yes</td>
<td>Rare</td>
<td>No</td>
</tr>
<tr>
<td>Microvascular complications</td>
<td>Yes</td>
<td>Yes</td>
<td>Rare</td>
</tr>
<tr>
<td>Macrovascular complications</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Microvascular Complications in Individuals with Diabetes > 10 Years Duration:

<table>
<thead>
<tr>
<th>Complication</th>
<th>CFRD</th>
<th>T1D/T2D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinopathy</td>
<td>15%</td>
<td>60%</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>16%</td>
<td>20-30%</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Gastropathy</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Macrovascular</td>
<td>0%</td>
<td>~60%</td>
</tr>
</tbody>
</table>

Schwarzenberg, Moran et al. *Diabetes Care*. 2007
Clinical Signs and Symptoms of CFRD:

- Excessive thirst or excessive urination
- Failure to gain or maintain weight despite nutritional intervention
- Failure to grow
- Delayed progression of puberty
- Chronic decline in pulmonary function

Outcomes:

- **Reduced survival**
  - In a study of 448 people with CF, less than 25% with diabetes survived to age 30, whereas nearly 60% of people without diabetes reached this age
    - Finkelstein et al *J Pediatr* 1988

- **Decreased pulmonary function**
  - Cross sectional analysis of 7,566 people enrolled in the European Epidemiologic Registry of CF found lower FEV1% in those with DM vs those without DM at all ages (72% vs 52%)
    - Koch et al *Pediatr Pulmonol* 2001
Oral Glucose Tolerance Test (OGTT)

- Fasting, 30 minute, 1 hour, 2 hour blood draws after glucose beverage
- Most sensitive way to detect CFRD without fasting hyperglycemia
- Early Identification is KEY!
  - High risk for progression to fasting hyperglycemia
  - High risk for excessive decline in pulmonary function

Glucose Tolerance Prevalence in Individuals with CF


- Normal glucose tolerance
- Impaired glucose tolerance
- CFRD without fasting hyperglycemia
- CFRD with fasting hyperglycemia
Insulin Secretion:

PS=pancreatic sufficient
DM=diabetes mellitus


* P<0.001 vs control
Insulin Therapy Improves BMI in CFRD Without Fasting Hyperglycemia:

- N= 81
- Individuals with CFRD without fasting hyperglycemia were treated with insulin vs. Repaglinide or placebo
- Insulin group showed improved BMI after one year of therapy whereas the group treated with Repaglinide did not

Screening Recommendations

- Use of A1C not recommended
- Screening: 2 hour OGTT
- Begin annual screening at age 10
- In-patient screening: Fasting, 2 hour post-prandial BS x 48 hours
- Screening for patients on continuous enteral feeds at time of gastrostomy feeding initiation, then monthly using SMBG
Diagnosis Recommendations

- 2 hour OGTT plasma glucose $\geq 200$ mg/dl
- Fasting plasma glucose $\geq 126$ mg/dl
- A1C $\geq 6.5$
- Test on 2 separate days to rule out laboratory error
- Diagnosis can be made during acute illness, when abnormal fasting plasma glucose or 2 hour post prandial levels persist for greater than 48 hours
Management Recommendations

- Refer to Endocrine (initially should be seen quarterly)
- Treatment with insulin
- Blood sugar monitoring minimum of three times daily
- Follow A1C quarterly (goal <7%)
- Nutrition management with carbohydrate counting (no calorie restriction)
Diabetes Complications

- Education regarding symptoms, prevention and treatment of hypoglycemia
- Measure blood pressure at every diabetes visit
- Annual monitoring for micro-vascular complications ($\geq 5$ years)
- Annual lipid profile (Pancreatic sufficient patients or if risk factors present)
LPCH CF Center Protocol

- **Annual screening:** 6 years and older with concurrent insulin levels

- **Home BG monitoring:** Individuals with impaired glucose tolerance

- **Referral to Endocrine:** Individuals with CFRD with and without fasting hyperglycemia

- **In-patient monitoring:**
  - Fasting, 2 hour post-prandial BG x 48 hours
  - 2 am, immediately post overnight GT feeds for individuals with newly placed gastrostomy tube feedings
What does more aggressive management mean?

- Routine screening with annual OGTT for patients aged ≥ 6 years
- Careful inpatient glucose monitoring and use of insulin as needed
- Early institution of intensive insulin therapy has become more routine in the last 5 years
- Pre-meal insulin is prescribed for those with CFRD without fasting hyperglycemia
Summary:

- CFRD is a challenging disease to diagnose and treat
- Earlier screening
- Improve the health and well being of our patients and families
Questions?
Thank you!