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The Unique Management of Cystic Fibrosis–Related Diabetes and the Importance of Glycemic Control

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ABSTRACT

Cystic fibrosis (CF) is a rare autosomal recessive lung disease that decreases the ability of chloride channels to function properly, leading to complications such as salt loss and mucus accumulation in different organs. Mucus accumulation leads to lung infections and decreased pancreatic function, nutrition, and sperm production. Treatment developments have prolonged the median life expectancy, but, with increasing age, a condition known as CF-related diabetes (CFRD) is more likely to develop. CFRD is a distinct condition that is different from type 1 and type 2 diabetes in key ways, including its pathophysiology, diagnosis, and management. It is essential for nurse practitioners in the primary-care setting to recognize these differences, because CFRD is becoming more common in CF patients. Obtaining glycemic control and recognizing its importance in patients with CFRD is especially significant, because glycemic control is correlated with lung function. This review focuses on recognizing CFRD and the rationale behind treatment differences.

Keywords: cystic fibrosis, diabetes

Currently, there are about 30,000 people in the United States who have been diagnosed with cystic fibrosis (CF), an autosomal recessive lung disease that decreases the ability of chloride channels to function properly.[1] This inherited chloride channel defect results in decreased salt levels through sweat loss and contributes to mucus accumulation in different organs, including the lungs and gastrointestinal tract. Patients are predisposed to abnormal colonization of microorganisms in the lungs, decreased pancreatic function, and diminished nutrition, and, in men, there is decreased sperm production.[1,2] CF-related diabetes (CFRD) is one of the many possible complications faced by patients with CF and represents the most prevalent comorbidity.[3] CFRD leads to increased hospitalization rates,[4] and even decreased pulmonary function.[3]

INTRODUCTION TO CFRD

Treatment developments for CF have prolonged patients' median life expectancy from 25 years in 1985 to 41.1 years in 2012.[1,5] CFRD becomes more likely as patients with CF age, occurring in 20% of adolescents with CF and 40% to 50% of adults with CF.[3] A major component of treatment for patients with CFRD is insulin, because achieving glycemic control has many benefits, such as improved lung function, weight gain, and survival.[3] Five studies within the last 6 years suggested that lung function is improved when glycemic control is established in CF patients.[6–10]

DIFFERENTIATING CFRD FROM TYPE 1 AND TYPE 2 DIABETES

CFRD shares aspects of type 1 and type 2 diabetes, but there are key differences.[11] The unique management of CFRD is tailored to control sugar levels while

keeping the CF stable.[2] Nurse practitioners (NPs) need to be aware of these differences to manage patients with CFRD in an appropriate manner. The most pressing issue in type 1 and type 2 diabetes is the development of microvascular and macrovascular complications, whereas more urgent concerns for CFRD patients include losing weight and lung function.[3]

DIAGNOSING CFRD

CF patients should be screened for CFRD yearly starting at age 10, according to the American Diabetes Association and the US Preventive Service Task Force, preferably by using the modified 2-hour 75-g oral glucose tolerance test (OGTT). Fasting glucose levels are drawn first, and 2-hour levels are drawn after the patient drinks a beverage containing 1.75 g/kg (up to 75 g maximum) of glucose after sitting quietly for 2 hours. Hemoglobin A_{1c} (HbA_{1c}) assessment is not the best screening measure because it can be falsely low in CF.[3] Although HbA_{1c} levels tend to be lower overall in patients with CF, levels are still sometimes drawn. Elevations in HbA_{1c} can indicate an increased risk for microvascular complications and may also identify trends in glycemic control.[3] The standard American Diabetes Association criteria used to diagnose diabetes in the general population is approved for use in healthy CF patients who have not had a CF exacerbation in at least 6 weeks.[3] The possible tests used to diagnose CFRD include: fasting glucose $\geq$ 126 mg/dL; 2-hour OGTT $\geq$ 200 mg/dL; and $HbA_{1c} \geq 6.5\%$. All 3 of these measurements must be repeated on an additional day to confirm elevated results. Elevated fasting glucose and HbA_{1c} can be used to confirm a diagnosis, but, when normal, the OGTT should be repeated.[3] If a patient has a random glucose of $\geq$ 200 mg/dL and also has polyuria and polydipsia, a confirmatory test is not necessary for diagnosis.[3] Patients with CFRD, with or without fasting hyperglycemia, should be treated with insulin, so isolating the type of CFRD is not essential for diagnosis.[3]

CF patients who are not considered stable outpatients, such as those receiving IV antibiotics, glucocorticoids, or enteral tube feedings, are diagnosed with CFRD using different criteria.[3] Acutely ill patients receiving IV antibiotics or glucocorticoids are diagnosed when their hyperglycemia (fasting glucose $\geq$ 126 mg/dL or 2-hour postprandial $\geq$ 200 mg/dL) continues for $>$ 48 hours; if the patient measures their own glucose, it must be verified by the lab before diagnosis. CF patients receiving enteral tube feedings are diagnosed with CFRD when their glucose is $\geq$ 200 mg/dL, at mid- or post-feed on 2 different nights; again, if the patient measures their own glucose, it must be verified by the lab before diagnosis.

LITERATURE REVIEW

Five separate studies, from 2007 to 2011, have identified a correlation between glycemic control and lung function in patients with CFRD. One cohort study at a single clinic used a longitudinal design[9] to examine 42 patients with CFRD treated in Liverpool, United Kingdom, over the period from 1993 to 2006. The study was attempting to identify the long-term effects of insulin on pulmonary status, nutritional status, and hospitalization rates, and was at that time the largest of its kind. Treatment for CF was standardized, comprising vitamin and enzyme supplements (the specific vitamins and supplements were not indicated), inhaled bronchodilators, chest physical therapy, antibiotics, mucolytic agents, and nutrition. Thirty-one of the 42 patients received short-acting insulin at least 3 times per day with meals, 9 of the 42 used both short-acting insulin with meals and basal insulin daily, and 2 of the 42 used daily basal insulin alone. Each patient acted as their own control after insulin treatment was initiated. Linear regression analysis was used to measure clinical change, with $P < .05$ considered significant. On average, body mass index (BMI), forced expiratory volume in 1 second (FEV_1), and forced vital capacity (FVC) improved significantly at 3 months and 1 year after treatment started. BMI remained significantly improved for 3 years and FVC for 2 years, although hospitalization rates were not reduced by insulin. FEV_1 did not remain elevated for as long as BMI and FVC; it took FEV_1, on average, 34 months to return to baseline, suggesting that lung deterioration is slowed when insulin is administered.

A matched study in Vancouver, British Columbia,[8] retrospectively compared the clinical outcomes of 40 patients with CFRD versus 40 patients with CF, but not CFRD, using their patients' data. FEV_1 and BMI