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Update on Nutritional Recommendations in Diabetes Related to Cystic Fibrosis

In people with cystic fibrosis (CF), carbohydrate metabolism disturbances, with the most prominent being cystic fibrosis-related diabetes (CFRD), are the most common non-pulmonary complications. Nutritional treatment for cystic fibrosis aims to achieve and maintain good nutritional status and prevent malnutrition, including both undernutrition and overweight/obesity. The importance of achieving good nutritional status is directly related to better lung function and, consequently, a better overall prognosis and survival. Respiratory failure is currently the leading cause of death in CF.

Dietary recommendations for people with Cystic Fibrosis (CF) have been based on a high-calorie and high-fat diet. The goal of this hypercaloric diet was to compensate for both the persistent fat malabsorption associated with pancreatic insufficiency (PI) and the increased energy expenditure. All of this to be able to reach the specific body mass index (BMI) recommendations: in children, BMI z-score of 50, in women BMI = 22 kg/m2, and in men BMI = 23 kg/m2.

Reaching the high energy needs of the "traditional" CF diet, of up to 150-200% of the daily caloric intake, has often resulted in poor quality and nutrient-poor dietary patterns, evidenced by the intake of foods high in saturated fats and added sugars, above the recommendations for the general population (1). But this eating pattern is associated with an increased cardiovascular risk and is a risk factor for the development of carbohydrate metabolism alterations in people with CF.

The most recent guidelines on the management of CF recommend including the evaluation of body composition, in addition to BMI, to define the appropriate nutritional status. When analyzing body composition, an inverse relationship is observed between the % of fat mass and pulmonary function measured with the volume of air expelled during the first second of forced expiration (FEV1); that is, the higher the % of fat mass, the worse the pulmonary function. On the contrary, there is a positive relationship between FEV1 and fat-free mass; that is, the higher the lean mass, the better the pulmonary function. The reduction of lean mass is associated with a decrease in pulmonary function (2). In addition, the evaluation of body composition may be more sensitive in the nutritional study of people with CF compared to BMI, given its link with insulin secretion (3).

NUTRITION IN PEOPLE WITH CYSTIC FIBROSIS

The composition of the diet of people with CF is key to achieving the best possible nutritional status and pulmonary function, in addition to delaying the development of carbohydrate metabolism alterations.

Carbohydrates (CHO): should be provided in the form of complex CHO, minimally processed and with high fiber content, avoiding simple CHO. This will help maintain better glycemic control, avoiding episodes of hyper- and hypoglycemia.

Fats: it is recommended to base their intake on monounsaturated fatty acids (olive oil, olives, avocado) and polyunsaturated fatty acids (PUFAs) (seed oil, oily fish), especially omega-3 fatty acids (DHA, EPA). Avoid saturated fatty acids and cholesterol that provide foods of animal origin or ultra-processed foods (3). The consumption of mono and polyunsaturated fats has beneficial effects on cardiovascular health, while saturated and trans fats increase cardiovascular risk. In people with CF, the intake of essential fatty acids, especially EPA and DHA, should be individually assessed, since a defect in the metabolism of PUFAs and an alteration of the arachidonic acid/docosahexaenoic acid (AA/DHA) ratio have been detected (4).

Proteins: protein requirements are higher than the general population due to various factors: chronic pro-inflammatory situation, respiratory distress or protein maldigestion derived from enzyme deficiency. Protein intake can come from high biological value proteins such as egg white, meat, dairy or fish (choosing oily fish such as sardines, anchovies, tuna or salmon gives us an extra supply of omega 3 fatty acids) and, also, from vegetable proteins, such as legumes or nuts.

Therefore, the diet of people with CF should be varied, including all food groups, and balanced, with a moderate increase in the content of healthy fats and proteins, and a consumption of complex CHO (5). The caloric and nutrient intake in each person should be adjusted to their nutritional status; this will help prevent both malnutrition and excess body fat.

In addition, in people with CF with high daily energy expenditure, the diet can be enriched with healthy foods and fats such as olive oil, olives, avocado/guacamole, nuts, seeds, cheese, hummus... If total energy requirements are not met with the enriched oral diet, it is recommended to introduce oral nutritional supplements (ONS), such as complete hypercaloric polymeric formulas.

Adequate hydration, throughout the day, and a sufficient salt intake are essential to »

THE DIET OF INDIVIDUALS WITH CF SHOULD BE VARIED, INCLUDING ALL FOOD GROUPS, AND BALANCED, WITH A MODERATE INCREASE IN HEALTHY FATS AND PROTEINS, AND A CONSUMPTION OF COMPLEX CARBOHYDRATES

THE GOAL IS TO IMPROVE OR MAINTAIN GLYCEMIC TARGETS, ACHIEVE WEIGHT CONTROL TARGETS, AND IMPROVE CARDIOVASCULAR RISK FACTORS

» avoid the increased risk of dehydration that people with CF have due to the alteration of the CF transmembrane conductance regulator (CFTCR) protein, especially infants and children, and in situations of high temperatures, intense physical exercise and/or fever.

Since diagnosis, in people with CF with PI, the guidelines recommend supplementation of fat-soluble vitamins: A, E, D and K. Vitamin D levels, along with adequate calcium intake, are essential for good bone health.

In people with CF and PI, whose pancreas does not produce the enzymes to digest food, attention must be paid to pancreatic enzyme replacement therapy (PERT). It is essential to have good adherence to PERT to be able to absorb all the nutrients ingested. Optimal digestion of macronutrients can play a role in the incretin hormone response and, therefore, in postprandial glycemia. If ONS are required, PERT will be increased depending on the amount of fat they contain. Optimizing PERT is essential in people with CF, especially if there are glycemic changes.

As an additional point to consider in people with CF, CFTCR protein dysfunction together with the dysbiosis of the intestinal microbiota produced, among others, by PERT, antibiotics and diets rich in saturated fats, favors intestinal permeability and inflammation. This inflammation affects glycemic control. A healthy diet, which includes foods rich in prebiotics (fiber: fruit, vegetables, legumes) and probiotics (yogurt, kefir, pickles), can help correct intestinal dysbiosis, reduce inflammation and improve glycemic control. Probiotic supplementation can be assessed individually, especially in those people with CF with frequent antibiotic treatments.

CYSTIC FIBROSIS-RELATED DIABETES (CFRD)

CFRD is an established complication in CF whose prevalence increases in parallel with increased life expectancy. Carbohydrate metabolism alterations begin in childhood and progress in relation to multiple factors. In common with other types of diabetes, it can present microvascular complications; specific to CFRD, it associates a significant decrease in pulmonary function, decreases survival due to pulmonary disease and favors a worse nutritional status.

Nutrition has a great impact on people with CF who develop CFRD and also on early carbohydrate changes. Malnutrition is a risk factor for CFRD, which constitutes another challenge in the planning and individualization of nutritional recommendations (6).

Diet quality has an impact on body composition, the risk of metabolic diseases and quality of life. The key is to individualize nutritional recommendations and weight goals. The goal is to improve or maintain glycemic goals, achieve weight control goals and improve cardiovascular risk factors (e.g. blood pressure, lipid profile, etc.).

Nutritional therapy is one of the cornerstones in the management of carbohydrate metabolism alterations in people with CF, including CFRD. Previous Clinical Practice Guidelines on Nutrition in CF postulated specific percentages of CHO, fats and proteins to create these diets. Although there is no evidence on the "best" balance between the different macronutrients in CFRD, the new guidelines suggest recommending a balanced diet based on the nutritional needs of each patient, with foods of low glycemic index (GI) and glycemic load to reduce glucose fluctuations (5) and avoid early postprandial hyperglycemia. Juices, sugary soft drinks and alcoholic beverages should be avoided.

It is important to keep in mind that CFRD and pulmonary function are interrelated: when there is no adequate glycemic control, pulmonary function worsens; during a pulmonary exacerbation, glucose levels are more unstable. Without forgetting that treatments used in CF, such as corticosteroids and bronchodilators, make diabetes control a challenge.

In people with CF scheduled lung transplant, it is especially important to have the best previous glycemic control and nutritional status.

THE ROLE OF NUTRITIONAL EDUCATION IN CFRD

Nutritional education in people with CF is very important throughout the different stages of life, including childhood. It should be personalized, with special emphasis on the quality, quantity and schedule of meals and their relationship with exercise and insulin dose. Clinical Practice Guidelines on nutrition in CF recommend that people with CF with CFRD be educated about the relationship between CHO and insulin action, to reduce postprandial glucose fluctuation and exposure to hyperglycemia. Education on the use of CHO counting, GI and glycemic load of foods should be individualized (5).

People with CFRD should be encouraged to maintain exercise and should be provided with information to prevent and/or resolve episodes of hypoglycemia. Avoid inappropriate dietary restrictions to improve glucose tolerance (7). People with »

CLINICAL PRACTICE GUIDELINES IN CF NUTRITION RECOMMEND EDUCATING INDIVIDUALS WITH CF AND CFRD ON THE RELATIONSHIP BETWEEN CARBOHYDRATES AND INSULIN ACTION TO REDUCE POSTPRANDIAL GLUCOSE FLUCTUATIONS AND EXPOSURE TO HYPERGLYCEMIA

» CFRD, by focusing more on food, may show some avoidance behavior and added risk of developing an eating disorder, especially in adolescence.

In people with CF with CFRD who need ONS to meet their daily nutritional requirements, it is recommended to use specific formulas for DM.

NUTRITION AND NEW THERAPIES IN PEOPLE WITH CF

In the last decade, the introduction and use of CFTR protein modulator drug therapy has resulted in increased survival and improvements in weight and BMI in many people with CF (8), which supports the new nutritional recommendations without hypercaloric diets to avoid overweight and its possible consequences (9). The mechanisms underlying weight gain are not well defined,but are likely to include a decrease in resting energy expenditure, systemic and intestinal inflammation and fat malabsorption (10). The technical data sheet indicates that these drugs should be consumed with foods rich in fat and avoid the consumption of grapefruit, bitter orange and St. John's wort.

The impact of these drugs on the appearance and progression of insulin secretion defects, insulin resistance and carbohydrate metabolism abnormalities is still under discussion, with promising results.

We cannot forget that modulator therapy is not eligible for all people with CF. It will depend not only on clinical factors, such as genotype or tolerance, but also on socio-economic factors, such as access to such treatment. D

CONCLUSIONS

Nutrition has a great impact on the development and progression of carbohydrate metabolism alterations in people with CF, both in childhood and adulthood. Maintaining good glycemic control is essential for good pulmonary function and better quality of life. The management of CFRD must be individualized and requires multidisciplinary care. In CF, continued nutritional education is essential to acquire healthy eating habits from childhood.

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