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RESEARCH ARTICLE

Effect of Protein Intake on Weight Gain and Growth in Cystic Fibrosis Patients

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ABSTRACT

Background and aim: despite the knowledge about the importance of adequate nutritional status in the health of patients with cystic fibrosis (CF), achieving protein intake recommendation remains a challenge. The influence of protein on anthropometric parameters in these patients needs to be better studied. The aim of the study was evaluated anthropometric changes after nutritional counselling to increase protein content in CF children and adolescents with low protein intake.

Methods: a prospective longitudinal study in 20 children and adolescents with CF. Food record of 3 consecutive days and anthropometric assessment were applied with an interval of 3 months. Patients with a protein intake <20% of the total daily caloric intake received nutritional counselling to increase protein content and patients with protein intake of ≥20% maintained their routine diet. Data were analyzed using the Generalized Estimating Equations (GEE) model.

Results: 15 patients (75%) had a daily protein intake of less than 20% of total daily calories at the first dietary assessment and received nutritional counselling. After 3 months, the protein content of the diet underwent a statistically significant increase, despite the other macronutrients and total daily calories. There was a significant improvement in z scores for weight ($p<0.001$), height ($p<0.001$) and body mass index (BMI) ($p=0.001$) compared to patients with adequate protein intake.

Conclusion: most CF patients did not meet the daily recommendation for protein intake. The reach of the proper protein intake allowed an increase in weight, height, and BMI.

Keywords: protein intake, nutritional status, cystic fibrosis, children, adolescents

Introduction

Cystic fibrosis (CF) is a genetic disorder and its phenotype results from mutations in the transmembrane conductance regulatory protein gene (CFTR), which leads to CFTR deficiency or dysfunction, changes that disable the transport of sodium and chloride ions through epithelial cells, and other membranes.[1] As a result, fluid transport is abnormal and mucous secretions become thick, thus impairing the function of organs such as the lungs, pancreas, liver, gallbladder, and intestines. Once in the lungs, thick mucus adheres to airway surfaces epithelium, which leads to impaired mucociliary clearance, an increased risk of inflammation, and infection. When they reach the pancreas, thickened secretions clog the intrapancreatic ducts, reducing the delivery of digestive enzymes to the intestines and impairing the absorption of essential nutrients.[2,3]

The knowledge about the importance of good nutritional status and its direct relationship with better lung function and, consequently, a better overall prognosis and survival in patients with cystic fibrosis has emerged in recent decades.[4] CF patients require high rates of energy and increased nutrient intake. The main cause of energy loss is malabsorption, often as a result of maldigestion due to reducing pancreatic enzyme activity (mainly pancreatic lipase) in the intestinal lumen below the threshold required for digestive functions (exocrine pancreatic insufficiency), which can be associated with other metabolic changes (e.g., intestinal inflammation, bacterial overgrowth, low bicarbonate production).[4,5] In addition, energy requirements are higher in CF patients due to persistent lung inflammation and associated infections. Therefore, achieving and maintaining an adequate nutritional status in these patients becomes a major challenge.[5]

Nutritional monitoring should be a priority in the management of patients with CF from the moment of diagnosis. The nutritional focus is a balanced diet with a specific nutrient distribution, according to individual requirements, and the maintenance of an age-appropriate growth pattern.[6,7] Historically, CF nutritional guidelines routinely recommended a diet rich in energy. Recently, attention has been drawn to monitoring macronutrient intake as well as total energy, with 35-40% from lipids, 40-45% from carbohydrates, and 20% from proteins in a total daily energy intake of 110–200% of that recommended for the healthy population of the same age group.[2,3]

Limited studies have investigated macronutrient intake other than fat in patients with CF.[8,9] In addition, CF patients may present an imbalance between protein degradation and synthesis, leading to loss of muscle mass, with an effect on respiratory muscles and consequent impairment of pulmonary function.[10]

Nutritional counselling, in this sense, has been highlighted in current guidelines to achieving a healthy diet with an adequate macronutrient distribution.[2,3,6] The protein content of the diet of patients with CF and its effects on nutritional status and health needs to be further studied. This study, therefore, aimed to evaluate anthropometric changes after nutritional counselling to increase protein content in CF children and adolescents with low protein intake.

Methods

Study Design And Participants

This is a prospective longitudinal study. Inclusion criteria were patients from 1 year to 17 years and 11 months with a diagnosis of CF, confirmed by two positive sweat tests, and who maintained regular clinical follow-up at the Hospital da Criança Santo Antônio (HCSA) in Brazil. Patients who did not appropriately complete the two nutritional assessments within a period of three months were excluded.

Data collect

The main variables studied were anthropometric data (weight, height, body mass index [BMI]) and food intake (calories, carbohydrates, proteins, and lipids). All anthropometric and dietary measures were taken in two moments: at inclusion in the study (baseline) and after three months.

Anthropometric data (weight and height) were measured in routine consultations by trained clinical staff using standard procedures and evaluated according to the references of the World Health Organization (WHO).[11,12] Weight was measured with a digital scale and height measured with a stadiometer.

Dietary assessment was performed through the analysis of food records for three consecutive days. The food records were obtained at baseline and three months post-nutritional counselling. Patients and their guardians were instructed by the nutritionist on the proper filling out of the form and sent it by email after completing the registration. Printed explanatory material, such as an example of a food record and a table of household measurements with equivalences in grams, was given to all participants, to guarantee the accuracy of the information recorded. Food records were analyzed by the nutritionist using the Dietbox Software[13] which expresses the daily caloric intake

along with the distribution of proteins, fats, and carbohydrates.

After the first food record analysis, the sample was divided into two groups: patients with daily protein intake ≥20% of the total caloric value and daily protein intake less than 20% of the total caloric value.

Patients who had a daily protein intake of less than 20% of the total caloric value, received a diet counselling with the aim of increasing the protein intake. This dietary advice was individually based on increasing the supply of protein-rich foods and/or increasing the size of their portions, and prioritizing proteins of high biological value. Patients with protein intake greater than or equal to 20% of total caloric value, routine nutritional counselling, based on current guidelines for macronutrient intake in pediatric patients with CF was maintained.

After three months, all patients were reassessed anthropometrically. In addition, a second dietary record was completed. All patients were instructed to maintain their routine clinical treatment, including use of CF-specific vitamin supplement and pancreatic enzymes.

Statistical analysis

Quantitative variables were described by mean and standard deviation and categorical variables by absolute and relative frequencies. The Generalized Estimating Equations (GEE) model was applied to analyze changes in percent energy from macronutrient intake (percent energy from carbohydrate, percent energy from protein, percent energy from fat) over time, and the relationships between percent energy from protein and growth, controlling for child age. The significance level adopted was 5% ($p<0.05$) and the analyzes were performed using the SPSS version 21.0 program.

Ethical aspects

All guardians provided written informed consent. The study was approved by the Research Ethics Committee of the HCSA under CAAE: 33300620.0000.5683.

Results

Twenty children and adolescents with cystic fibrosis appropriately completed both nutritional assessments within a three-month period and participated in the study. Eleven patients (55%) were female. The mean age was 9.7±4.9 years and the BMI was 0.27± 1.32. The characteristics of the sample at baseline are shown in table 1.

Table 1 – Baseline sample characteristics

Characteristics	
N	20
Age, years (mean±SD)	9.7 ±4.9
Female, N (%)	11 (55)
Z score W/A (mean±SD)	0.42 ± 1.37
Z score H/A (mean±SD)	-0.66 ± 1.51
Z score BMI/A (mean±SD)	0.27 ± 1.32

W/A= weight to age; H/A= height to age; BMI/A= body mass index to age

The average calorie intake and the distribution of macronutrients as a percentage of the total energy value of the patients' diet are shown in Table 2. At baseline, none of the macronutrients or calories were in accordance with the practical guidelines for CF. After a period of three months, only the protein content of the diet changed significantly ($p<0.001$), closely approaching the guidelines recommendations.

Table 2: Comparison of daily macronutrients and energy consumption between the two moments in all patients

Nutrient	Baseline	Post 3 months	Difference	p*
	Mean ± SD	Mean ± SD	(95% CI)*	
Protein†	16.3 ± 3.9	19.9 ± 1.7	3.56 (1.89 to 5.23)	<0.001
Carbohydrates†	54.5 ± 10.1	50.5 ± 7.6	-4.05 (-8.25 to 0.15)	0.059
Fat†	28.9 ± 10.0	29.2 ± 6.7	0.33 (-4.43 to 5.08)	0.893
Calories	1738 ± 441	1948 ± 515	210.5 (-12.4 to 433)	0.064

† % of total calories * Generalized Estimating Equations (GEE) model

Table 3 shows the change in weight, height, and BMI indicators for age after three months, according to the protein content of the patients' diet. Most patients (N=15; 75%) had a daily protein intake of less than 20% of total calories in the first dietary assessment and received nutritional counselling to increase the intake of this macronutrient. After three months, there was a significant improvement in the protein content of the diet in patients from six years, with no changes in the content of carbohydrates, lipids and total calories (Table 4), which resulted in an improvement in all anthropometric indicators of nutritional status (z score W/A 0.37 (0.17 to 0.58), p<0.001; z score H/A 0.28 (0.16 to 0.40), p<0.001, and z score BMI/A 0.41 (0.16 to 0 .66), p=0.001).

Table 3: Comparison of nutritional status between the two moments according to protein consumption group

Protein content†	Nutritional indicator	Baseline Mean ± SD	Post 3 months Mean ± SD	Difference (95% CI)*	p*
<20% (n=15)	Z score W/A	0.48 ± 1.54	0.85 ± 1.61	0.37 (0.17 to 0.58)	<0.001
	Z score H/A	-0.66 ± 1.57	-0.38 ± 1.47	0.28 (0.16 to 0.40)	<0.001
	Z score BMI/A	0.46 ± 1.23	0.86 ± 1.15	0.41 (0.16 to 0.66)	0.001
≥20% (n=5)	Z score W/A	0.23 ± 0.72	0.34 ± 0.77	0.11 (-0.04 to 0.25)	0.143
	Z score H/A	-0.64 ± 1.49	-0.48 ± 1.64	0.15 (-0.15 to 0.46)	0.324
	Z score BMI/A	-0.30 ± 1.57	0.02 ± 1.48	0.32 (-0.18 to 0.82)	0.215

* W/A= weight to age; H/A= height to age; BMI/A= body mass index to age † % of total calories
* Generalized Estimating Equations (GEE) model

Table 4: Comparison of macronutrient consumption between the two moments according to age group in patients with protein consumption <20%

Age group	Nutrient	Baseline Mean ± SD	Post 3 months Mean ± SD	Difference (95% CI)*	p*
Up to 5 years	Protein†	18.9 ± 0.8	20.1 ± 1.2	1.23 (-0.27 to 2.74)	0.108
	Carbohydrates†	48.2 ± 7.5	45.3 ± 13.4	-2.85 (-10.9 to 5.17)	0.487
	Fat†	32.9 ± 7.8	34.8 ± 12.0	1.91 (-4.83 to 8.66)	0.578
	Calories	1671 ± 456	1534 ± 313	-136.7 (-526 to 253)	0.492
6 to 10 years	Protein†	14.8 ± 3.8	19.6 ± 1.4	4.85 (1.96 to 7.74)	0.001
	Carbohydrates†	55.2 ± 7.7	49.8 ± 6.1	-5.47 (-12.5 to 1.52)	0.125
	Fat†	29.7 ± 9.3	29.4 ± 4.9	-0.31 (-8.42 to 7.79)	0.940
	Calories	1837 ± 198	2045 ± 416	208.3 (-91.8 to 508)	0.174
From 10 years	Protein†	16.9 ± 4.4	19.7 ± 2.6	2.78 (0.09 to 5.46)	0.043
	Carbohydrates†	57.6 ± 11.5	54.5 ± 5.1	-3.04 (-9.18 to 3.11)	0.333
	Fat†	25.2 ± 10.8	25.8 ± 4.2	0.60 (-6.63 to 7.84)	0.870
	Calories	1758 ± 613	2041 ± 707	282.2 (-204.3 to 768)	0.255

† % of total calories * Generalized Estimating Equations (GEE) model

Discussion

The present study demonstrated that most children and adolescents with cystic fibrosis had an inadequate protein intake, less than 20% of total calorie needs. After nutritional counselling, in patients older than six years, we found a significant increase in the protein content of the diet, closely approaching the nutritional recommendations of the current guidelines for CF. In addition, an

improvement was observed in all anthropometric parameters of nutritional status, only with the increase of protein, without alteration of the other macronutrients.

Parallel with advances in the understanding of the cystic fibrosis and its therapy in recent decades, adequate nutrition and growth have strengthened as key factors for better outcomes in the management of the disease.[4,5] Currently, the challenges of effective nutritional therapy for patients with CF revolve around issues related to energy imbalance, macronutrient distribution, diet composition, and adherence to recommendations.[2]

Achieving dietary goals of calories and macronutrients can be difficult to manage. Historically, the CF nutritional guidelines recommended a high-calorie diet, with no fat restriction as fundamental for a good nutritional status.[14] However, nutritional imbalances and anthropometric deficits remain frequent in children and adults with CF nowadays, in addition to current concerns about overweight and obesity rates.[6] More recently, emphasis has been placed on the importance of adequate distribution of macronutrients and the fundamental role of protein content.[2,14,15]

Research on macronutrient benchmarks in CF patients are scarce and focusing primarily on energy intake is not enough to optimize diet and nutritional status.[16] A retrospective study that evaluated dietary intake through a 3-day food record of 86 paediatric patients with CF found a mean contribution of fat, carbohydrate, and protein to the total caloric intake of 35%, 50%, and 14%, respectively.[8] In a cross-sectional study with CF paediatric patients from six European centres, Calvo-Lerma et al. observed a mean protein intake of 14% of the total energy, and 51% and 34% for carbohydrates and lipids respectively.[17] In the study on the effectiveness of a self-management mobile app to support CF patients to achieve the dietary goals established by the CF nutrition guidelines showed that the distribution of macronutrients better approached the recommendations after six months of using the app. The change, although significant, was not enough to meet the protein recommendation, reaching only 15.5% of the total energy intake.[18]

Protein intake is crucial for growth, promotes muscle mass gain, and is related to lung function, which may be especially relevant given the increased life expectancy of patients with CF.[2,6] The cumulative deficit of proteins may negatively affect growth and development[19,20] and the consumption of adequate amounts is essential to meet the metabolic demand and both total nitrogen and essential amino acids requirements.[21] Currently, high-quality protein intake is strongly recommended, in addition to an individualized anthropometric assessment, as a way of inducing fat-free mass gain and preventing central obesity. Protein intake should be routinely monitored to ensure that target amounts are achieved.[22]

However, the 20% protein recommendation seems difficult to achieve and limited studies focus on the protein content and its effect on the nutritional status of paediatric patients with CF.[23] Our study associated protein intake with the anthropometric assessment of patients. None of the macronutrients nor the total daily calorie content were in accordance with the nutritional guidelines for CF in the first food record and 75% of patients had a daily protein intake of less than 20% of total calories. After nutritional counselling focused on dietary protein in those patients with low protein intake, there was an important increase in the protein content and an improvement in all indicators of nutritional status. There was no change in total caloric intake or in carbohydrate and fat content, which reinforces the effect of protein on weight gain and growth in these patients. In a study with 75 preschoolers, the percent of energy from protein was correlated with height growth, but not with weight.[24]

In this sense, it is urgent that adequate dietary composition be a goal to be achieved in the individual nutritional approach of patients with CF. Precise indications of macronutrient intake should be provided as a starting point for nutritional intervention, with particular attention to protein intake.[6] It is not appropriate to simply assume that protein recommendation is met when energy requirement has been met.[25]

The difficulty in improving the nutritional status of patients with CF is known. Different interventions have been used, such as oral supplementation and tube feeding, but little has been addressed in nutrition education to promote dietary changes and its impact on nutritional status.[26] Current evidence points to the high relevance of nutritional counselling to achieve specific dietary goals for CF through a healthy and balanced diet, properly distributed. Our results show the early positive impact that nutritional counselling can have in this regard, with repercussions on growth.

The study had several limitations. The most important concern is the sample size. Completing the food record for three consecutive days required the involvement and availability of family members

and the complete accuracy of the information recorded cannot be guaranteed. However, all study participants received detailed verbal and written guidance regarding the completion of the form, to increase the accuracy of the record. Another limitation was the need to send the registration by email. Also, the quality of the food ingested was not evaluated, since it was not among the objectives of the study. On the other hand, the results are strengthened by processing data from food records by a CF dietist using nutritional software.

Conclusion

Finally, this study revealed macronutrient inadequacies in the diet of paediatric patients with CF and highlighted the important role of protein content in improving weight gain and growth. An individual assessment and proactive nutritional counselling based on CF guideline recommendations are critical to achieving dietary goals and can positively impact health and growth. Large, well-designed clinical trials are needed to confirm these findings.

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