The Effects of Dietary Counseling on Children with Food Allergy: A Prospective, Multicenter Intervention Study

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ABSTRACT

Although dietary counseling is generally recommended in children with food allergy (FA), its effect on the nutritional status of these patients has not yet been evaluated. Our nonrandomized multicenter prospective intervention study was undertaken to investigate the effects of dietary counseling on children with FA. Anthropometric data, dietary intakes, and laboratory biomarkers of nutritional status were evaluated in children with FA (aged 6 to 36 months) before and after dietary counseling, by multidisciplinary teams composed of pediatricians, dietitians, and nurses. Ninety-one children with FA (49 boys and 42 girls; mean age 18.9 months, 95% CI 16.5 to 21.3) were evaluated; 66 children without FA (41 boys and 25 girls; mean age 20.3 months, 95% CI 17.7 to 22.8) served as controls providing baseline values only. At enrollment, energy and protein intakes were lower in children with FA (91 kcal/kg/day, interquartile range [IQR]=15.1, minimum=55.2, maximum=130.6; and 2.2 g/kg/day, IQR=0.5, minimum=1.5, maximum=2.7, respectively) than in children without FA (96 kcal/kg/day, IQR=6.1, minimum=83.6, maximum=118.0; and 4.6 g/kg/day, IQR=1.2, minimum=2.0, maximum=6.1, respectively; $P<0.001$). A weight to length ratio <2 standard deviations was more frequent in children with FA than in children without FA (21% vs 3%; $P<0.001$). At 6 months following dietary counseling, the total energy intake of children with FA was similar to the baseline values of control children. Dietary counseling also resulted in a significant improvement of their anthropometric and laboratory biomarkers of nutritional status. The results of our study support the crucial role of dietary counseling in the clinical management of children with FA.
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FOOD ALLERGY (FA) IS A MAJOR HEALTH ISSUE FOR children living in Western countries.[1] Management of FA consists of strict elimination of the offending allergen from the diet until tolerance is acquired.[1] FA predominates in early childhood during the vulnerable period of rapid growth, when inadequate nutrition could have an influence on adult health. Eight foods (cow's milk, hen's egg, soy, peanuts, tree nuts, wheat, fish, and shellfish) account for more than 90% of childhood cases of FA.[1] Most of these foods have a high nutritional value and are affordable for children living in Western countries. Inappropriate elimination diets in children with FA can induce vitamin and mineral deficiencies, anemia, rickets, failure to thrive, and kwashiorkor.[2-4] Dietary counseling is recommended to prevent these conditions,[1,5,6] but the effect of this service on the nutritional status of patients with FA has never been explored. The aim of our study was to investigate the effects of dietary counseling on growth, energy intakes, and on laboratory biomarkers of nutritional status in children with FA.

METHODS

Study Design

Our nonrandomized, prospective, multicenter intervention study was conducted between September 2006 and March 2008 in outpatient children with FA (aged 6 to 36 months) who were following an elimination diet without dietary counseling for at least 60 days. These children were consecutively referred for consultation to two tertiary centers for pediatric allergy and nutrition (located in Milan and Naples, Italy, respectively). Exclusion criteria were a history of prematurity (<37 gestational weeks), systemic diseases, cardiovascular diseases, hematologic diseases, chronic respiratory diseases, psychiatric disorders, renal failure, neurologic impairment, active tuberculosis, autoimmune diseases, immunodeficiency, chronic inflammatory bowel diseases, gastroesophageal reflux disease, celiac disease, cystic fibrosis, metabolic or endocrine diseases, genetic defects, malignancies, and malformations of the gastrointestinal or the urinary tract.

At each center, the children with FA were seen by a pediatrician and a dietitian who evaluated the medical history and clinical condition and verified the diagnosis of FA according to standard criteria.[1,7] If the diagnosis of FA was confirmed, the pediatrician invited the parents to participate in the study. When parents provided written informed consent to participate in the study, they were asked to complete, prospectively, a 3-day food record in the form of a printed chart and to return the chart to the center within 1 week, when the enrollment visit (T0) was planned. The dietitian explained to parents how to record the amount and type of foods and drinks consumed by the child over a period of 3 consecutive days, including 2 weekdays and 1 weekend day. The chart also contained instructions about how to record the food consumed and how to measure food using graduated bowls, cups, dishes, and spoons. At the enrollment visit (T0) and 2 (T1), 4 (T2), and 6 months (T3) thereafter, the children with FA were evaluated by a multidisciplinary team composed of a pediatrician, a nurse, and a dietitian.

During the same period (namely, between September 2006 and March 2008) healthy children without FA (aged 6 to 36 months) consecutively evaluated at the centers before undergoing minor surgical procedures (eg, penile manipulation, inguinal hernia repair, and cyst excisions) were enrolled as nonmatched controls. The same exclusion criteria applied to the control group of children. Their parents, after providing informed consent, received instructions on how to complete the 3-day food record for the child. The control children were examined only at T0 by a multidisciplinary team.

At T0, the children of the two groups were evaluated when they were free of infectious diseases, medication use, trauma, vomiting, and diarrhea during the previous 3 weeks. Weight, length or height, and head circumference were measured using standard procedures.[8] Anthropometric indexes (*z* score for weight, *z* score for length/height, and *z* score for head circumference) were determined using the Euro-Growth References.[9,10] The medical record of each child was recorded on a clinical chart. The study was approved by the Ethics Committee of each Institution and was registered in Clinical Trials Protocol Registration System (ID no: NCT01583907).

Dietary Assessment and Counseling

At T0, the dietitian examined the dietary history and reviewed the 3-day food records of the two groups of children. The assessment of dietary history included the child's food preferences, food aversions, and behavior problems at mealtimes. Diaries were analyzed using specific software based on the Italian food composition tables (Winfood Pro 2.5, 2006, Medimatica Srl). At this enrollment visit, the children with FA underwent a personalized dietary counseling session. Dietary counseling was based on the evaluation of body weight, length/height, weight to height ratio, and head circumference; rate of required catch-up growth (based on weight to height ratio or standard deviation [SD] scores) and its feasibility depending on the patient's current dietary intake and allergen restriction; and protein and energy requirements.

The dietitian suggested dietary changes based on the 3-day food record. The dietitian counseled parents about issues that could arise during an elimination diet and how to replace the allergenic foods with an alternative source of nutrients to reach the daily recommended intake for Italian children adjusted for age and sex.[11] In patients with cow's milk allergy (CMA), the daily amount of substituted formula was determined, and an increase of formula concentration was proposed when necessary. In children affected by other forms of FA or by multiple FA, a list of antigenic foods was given to the parents, and inappropriate elimination of other foods was discouraged. When necessary, the total energy intake was customized according to calculated needs for catch-up growth. A fixed diet was never ordered, the families were encouraged to gradually introduce small changes to improve the child's diet. The key words and phrases used during dietary counseling were emphasized to encourage discussion about the food-related topics at home. Six months later (ie, at T3) the parents of the children with FA were asked to complete another 3-day food record that was also reviewed and edited by the dietitian.

Laboratory Measurements

At T0 a venous blood sample was collected from children with FA and from healthy controls (before the minor surgical procedures) to determine serum biomarkers of nutritional status, namely, hemoglobin, iron, albumin, total cholesterol, triglycerides, calcium, phosphorus, and zinc.[8] Plasma fatty acid levels were also determined by capillary gas chromatography after lipid extraction according to Folch and colleagues.[12] A second blood sample was collected 6 months later (ie, at T3) only from children with FA. Blood was sampled after an overnight fast.

Statistics

Eighty-five patients were required to obtain a power of the study of 90%, a type 1 error of 0.05 by two-tailed test. This estimate assumes a mean increase of the *z* score for weight after nutritional intervention of 0.5 (from −0.5 at T0 to 0.0 at T3, with an SD of 1), whereas 60 per group were required (power of the study of 90%, type 1 error of 0.05 by two-tailed test) assuming a difference of 1 between children without FA (0.5±1.5) and patients with FA (−0.5±1.5) in the *z* score for weight at T0. These computations were based on the expectations arising from the results of a preliminary open trial. For continuous variables, groups were compared using the test of equality of means. The χ^2 test and Fisher's exact test were used for categorical variables. A multivariate analysis using the general linear model for repeated measures was used to evaluate the influence on the primary study outcome of the following variables: age, sex, allergen, single or multiple FA, duration of exclusion diet before enrollment, age at diagnosis of FA, symptoms, and type of formula. When necessary, comparisons were performed with nonparametric tests (ie, Mann Whitney *U* test). Results were reported as means and 95% CI and as median and interquartile range (IQR) plus minimum and maximum range due to nonnormal distribution (established by the Kolmogorov test). The level of significance for all statistical tests was two-sided ($P<0.05$). All data were collected in a dedicated database and analyzed by a statistician blinded to patients' group assignment with SPSS version 13.0 for Windows (2004, SPSS Inc).

RESULTS AND DISCUSSION

From September 2006 to March 2008, 107 children with suspected FA were considered for the study. Nine patients were excluded because of concomitant other diagnoses (4

celiac disease, 2 Down syndrome, 1 cystic fibrosis, 1 inflammatory bowel disease, and 1 primary immunodeficiency). Six children were excluded because of unconfirmed FA, and one was excluded because of an incorrect exclusion diet (persistence of the offending food allergen in the diet). Ninety-one children (49 boys and 42 girls; mean age 18.9 months, 95% CI 16.5 to 21.3) with confirmed FA were enrolled. Six patients were lost to follow-up after the second visit. Thus, 85 children with FA completed the study. For comparison, 66 children without FA (41 boys and 25 girls; mean age 20.3 months, 95% CI 17.7 to 22.8) who were being evaluated at the centers before undergoing minor surgical procedures (penile manipulation in 40 children, inguinal hernia repair in 18 children, and cyst excisions in eight children) were evaluated at T0 only during the same study period.

The baseline demographic and clinical characteristics of children with FA are reported in Table 1. Fifty (54.9%) had received a prescription of exclusion diet from their family pediatrician, and 41 (45.1%) from physicians working in other centers. No child with FA had received dietary counseling before enrollment. Eighty patients were affected by CMA. Among these, 23 received extensively hydrolyzed casein formula, 20 received soy-based formula, 9 received rice formula, 6 received extensively hydrolyzed soy formula, 5 received extensively hydrolyzed whey protein formula, 4 received amino acid-based formula, and 3 received hydrolyzed rice-based formula. Ten children with CMA were not receiving any hypoallergenic substitute formula. Substitute formulas were not changed during the study in any child. Dietary supplementation was not administered in any child with FA.

At T0, a weight/length ratio below 2 SD was observed in a significantly higher percentage of children with FA compared with healthy children ($P<0.001$). No overweight was observed in the two groups at T0. After receiving dietary counseling a progressive decrease of the percentage of children with FA with a weight/length ratio below 2 SD was observed. At T3 the percentage of children with FA with weight/length ratio below 2 SD became similar to the healthy children so the difference between the two groups was not longer significant (see the Figure). The *z* scores for weight, length/height, and head circumference were significantly lower in patients with FA than in controls at T0 (see the Figure). After receiving dietary counseling, a progressive improvement of all the *z* scores was observed in children with FA (see the Figure).

The counseling procedure was well accepted by the parents of children with FA, as demonstrated by the low dropout rate. The return rate of the 3-day records was 100% for both control subjects and intervention patients at baseline and 93.4% at T3 for intervention group participants.

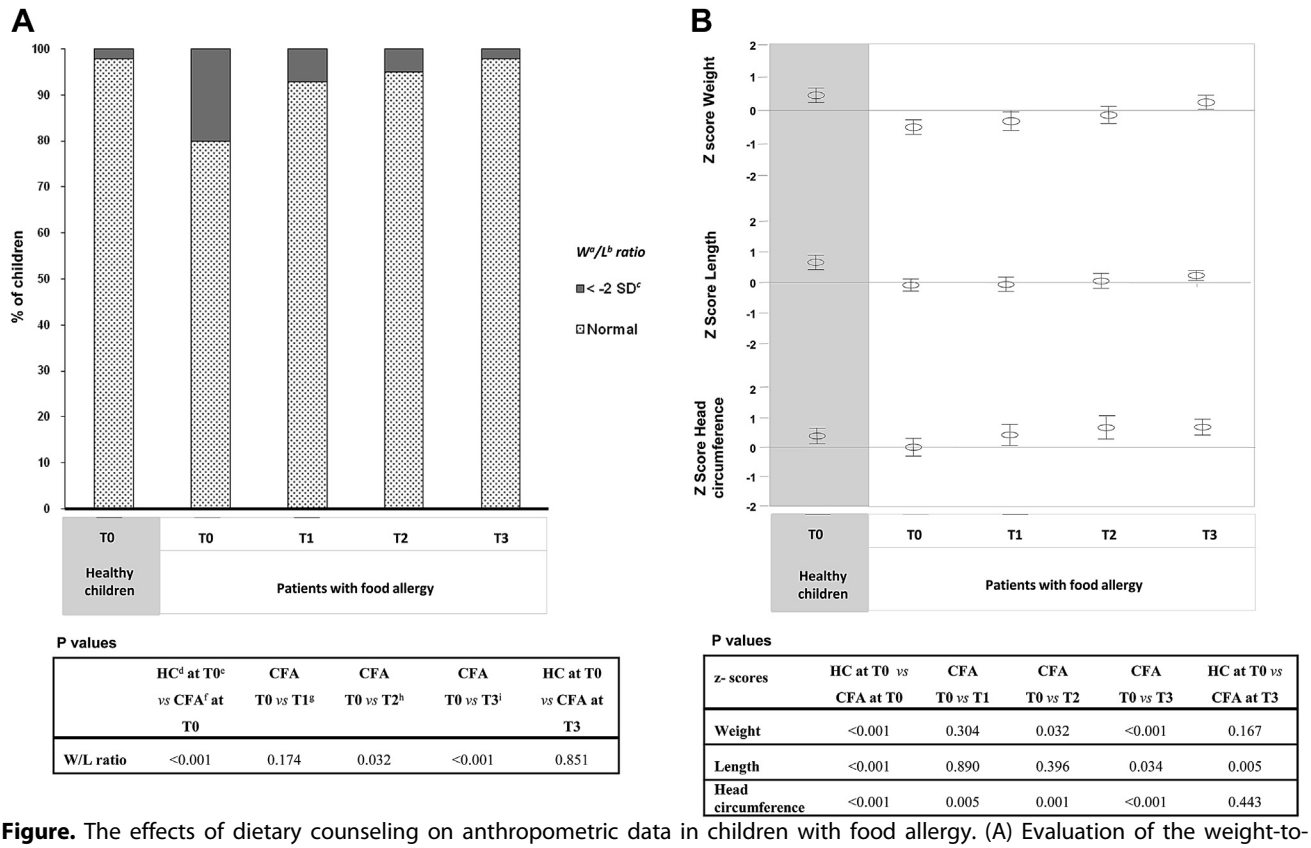
At baseline (T0), the analysis of the 3-day food record revealed significantly lower energy, protein, calcium, and zinc intakes in children with FA compared with healthy controls (Table 2). After 6 months of dietary counseling, there was a significant increase in energy, carbohydrate, protein, iron, fiber, calcium, and zinc intake in children with FA vs baseline (Table 3).

At T0 a blood sample was obtained in 85 children with FA and in 66 healthy controls. Then at T3 a new blood sampling was performed only in children with FA (78 of 85; 91%), but not in healthy children. At T0, the median values of all laboratory parameters were within normal range in both groups of children. Some FA patients presented abnormal values; the percent of FA participants with abnormal values of hemoglobin (10.5% vs 1.3%; $P=0.014$), iron (10.5% vs 5.9%; $P=0.02$), albumin (10.5% vs 2.6%; $P=0.043$), and zinc (23.3% vs 3.8%; $P<0.001$) significantly decreased at T3.

At T0, children with FA and healthy controls had similar levels of plasma saturated fatty acids (median=35.4, IQR=7.5 [minimum-maximum=26.3-48.2] vs median=34.6, IQR=3.3 [minimum-maximum=31.4-39]; $P=0.762$), whereas the concentrations of monounsaturated and polyunsaturated fatty acids differed between the two groups. In fact, children with FA had a higher concentration of monounsaturated acids (median=32.4, IQR=96.8 [minimum-maximum=20.2-137.9] vs median=22.9, IQR=3.4 [minimum-maximum=17.7-28.4]; $P<0.001$) and a lower concentration of total polyunsaturated fatty acids (median=34.2, IQR=5.2

Table 1. Baseline demographic and clinical characteristics of children with food allergy (N=91) enrolled in a prospective, multicenter intervention study evaluating the effects of dietary counseling

Characteristic	Result
Demographics	
Age, mo (95% CI)	18.9 (16.5-21.3)
Male, n (%)	49 (53.8)
Clinical records	
Age at symptoms onset, mo (95% CI)	8.5 (6.9-10.7)
Duration of elimination diet before enrolment, mo (95% CI)	10.8 (8.0-13.9)
Symptoms	*n (%)*
Gastrointestinal	53 (58.2)
Vomiting	19 (20.8)
Chronic diarrhea	27 (27.9)
Hematochezia	7 (7.7)
Cutaneous	53 (58.2)
Atopic dermatitis	49 (53.8)
Urticaria-angioedema	4 (4.3)
Respiratory	4 (4.3)
Asthma	4 (4.3)
Anaphylaxis	1 (1.1)
Allergens	
Cow's milk	80 (87.9)
Hen's egg	45 (49.4)
Soy	7 (7.6)
Fish	7 (7.6)
Tomato	6 (6.6)
Wheat	5 (5.5)
Legumes	4 (4.3)
Rice	3 (3.3)
Multiple food allergy	42 (46.1)



P values

	HC[d] at T0[e] vs CFA[f] at T0	CFA T0 vs T1[g]	CFA T0 vs T2[h]	CFA T0 vs T3[i]	HC at T0 vs CFA at T3
W/L ratio	<0.001	0.174	0.032	<0.001	0.851

P values

z- scores	HC at T0 vs CFA at T0	CFA T0 vs T1	CFA T0 vs T2	CFA T0 vs T3	HC at T0 vs CFA at T3
Weight	<0.001	0.304	0.032	<0.001	0.167
Length	<0.001	0.890	0.396	0.034	0.005
Head circumference	<0.001	0.005	0.001	<0.001	0.443

Figure. The effects of dietary counseling on anthropometric data in children with food allergy. (A) Evaluation of the weight-to-length (W/L) ratio in children without food allergy (healthy children [HC]) and in children with food allergy (CFA) at enrollment (T0) and at 2 (T1), 4 (T2), and 6 (T3) months of follow-up. (B) *z* scores for weight, length, and head circumference in children without food allergy (healthy children [HC]) and in children with food allergy (CFA) at enrollment (T0) and at 2 (T1), 4 (T2), and 6 (T3) months of follow-up. [a]W=weight. [b]L=length. [c]SD=standard deviation. [d]HC=healthy children. [e]T0=enrollment; [f]CFA=children with food allergy. [g]T1=follow-up after 2 months. [h]T2=follow-up after 4 months. [i]T3=follow=up after 6 months.

[minimum-maximum=25.9-48.2] vs median=42.4, IQR=3.1 [minimum-maximum=37.7-46.5]; $P<0.001$) compared with children without FA at baseline. In children with FA the values of monounsaturated fatty acids and of total polyunsaturated fatty acids changed slightly, but not significantly if compared with baseline values (median=30.4, IQR=3.3 [minimum-maximum=23.6-32.4] vs median=35, IQR=4.6 [minimum-maximum=31.2-40.2]). Table 3 shows the plasma levels of each polyunsaturated fatty acid observed in the study population. At T0, α-linolenic acid and eicosapentaenoic acid levels were similar in the two groups, whereas the levels of linoleic acid, di-homo-γ-linolenic acid, arachidonic acid, and docosahexaenoic acid were significantly lower in children with FA than in controls. At T3, children with FA showed a significant increase of arachidonic acid, eicosapentaenoic acid, and docosahexaenoic acid plasma levels, whereas di-homo-γ-linolenic acid, linoleic acid, and α-linolenic acid remained stable (Table 3).

Multivariate analysis showed that the significant improvement of *z* score values for weight ($P<0.001$) observed after 6 months of dietary counseling (T3) was not influenced by age, sex, allergen, single or multiple FA, duration of exclusion diet before enrollment, age at diagnosis of FA, symptoms, or type of formula.

Growth is considered the best and simplest indicator of nutritional status.[13] Acute malnutrition is commonly defined by a weight to height ratio <-2 SD.[13] The prevalence of acute malnutrition during the previous 10 years at hospital admission in children in Germany, France, the United Kingdom, and the United States varied between 6% and 14%.[14] The results of our study show that suboptimal growth accompanied by a suboptimal intake of energy is frequent in children affected by FA. The latter finding is in agreement with previous reports.[15,16] The concern about suboptimal energy intake is pressing also given the increasing prevalence of FA in Western countries.[1] Early growth retardation has been shown to predict longitudinal growth, thereby increasing a child's vulnerability to short stature later in life, and also possibly leading to reduced IQ, poor arithmetic performance, and altered work habits.[17-19] The results of our study show that poor growth in children with FA can be positively managed by personalized dietary counseling. Recent findings on the effect of least-restrictive diets, including baked milk or hen's egg,[20-22] or new extensively hydrolyzed cow's milk protein formula containing probiotics,[23,24] on disease duration open new possibilities of dietary intervention for children with FA.

Nutritional biomarkers also improved during our study. In accordance with previous evidence,[25] the fatty acids profile was altered in children with FA. The low level of polyunsaturated fatty acids warrants particular attention. From a qualitative standpoint, many children in our study were allergic to foods containing n-3 polyunsaturated fatty acids

Table 2. Energy and nutrient intakes in children with food allergy (aged 6 to 36 mo) at baseline (T0) and after 6 mo of dietary counseling (T3) compared with those observed in age-matched healthy children from a prospective, multicenter intervention study evaluating the effects of dietary counseling

	Healthy Children at T0 (N=66)			Patients with Food Allergy						*P* Value		
				T0 (n=91)			T3 (n=85)					
Nutrient	Median	IQR[a]	Minimum-maximum	Median	IQR	Minimum-maximum	Median	IQR	Minimum-maximum	Patients with food allergy at T0 vs healthy children at T0	Patients with food allergy at T0 vs at T3	Patients with food allergy at T3 vs healthy children at T0
Energy intake (kcal/kg/d)	96	6.1	83.6-118.0	91	15.1	55.2-130.6	97.3	19.6	73.9-135.7	<0.001	0.003	0.876
Carbohydrate (g/kg/d)	4.9	1.6	2.5-7.2	5.1	1.4	3.0-8.8	6.0	2.1	2.6-8.3	0.583	0.002	<0.001
Fat (g/kg/d)	4.2	0.6	3.2-7.0	3.8	1.4	1.7-6.3	3.6	0.9	2.5-5.4	0.407	0.117	0.002
Protein (g/kg/d)	4.6	1.2	2.0-6.1	2.2	0.5	1.5-2.7	3.6	0.9	2.3-5.1	<0.001	<0.001	<0.001
Fiber (g/d)	7.2	2.7	2.1-11.3	5.8	8.2	0.0-7.2	11.2	6.2	1.3-17.9	0.242	0.006	0.003
Calcium (mg/d)	848.3	306.9	328.3-1,309.7	314.4	285.6	114.5-690.1	600.0	246.9	250.0-971.9	<0.001	0.001	0.002
Iron (mg/d)	7.0	7.0	1.7-15.9	6.1	4.0	2.7-10.9	8.0	3.1	4.2-17.7	0.279	0.034	0.458
Zinc (mg/d)	4.1	0.2	4.0-4.5	3.0	1.5	2.5-4.0	4.5	0.9	4.0-5.0	0.009	0.004	0.106

[a]IQR=interquartile range.

Table 3. Plasma polyunsaturated fatty acids levels in children with food allergy (aged 6 to 36 mo) at baseline (T0) and after 6 mo of dietary counseling (T3) compared with those observed in age-matched healthy children from a prospective, multicenter intervention study evaluating the effects of dietary counseling

	Healthy Children at T0 (n=66)			Children with Food Allergy						*P* Value		
				T0 (n=85)			T3 (n=78)					
Nutrient	Median[a]	IQR[b]	Minimum-maximum	Median	IQR	Minimum-maximum	Median	IQR	Minimum-maximum	Patients with food allergy at T0 vs healthy children at T0	Patients with food allergy at T0 vs at T3	Patients with food allergy at T3 vs healthy children at T0
Linoleic acid (18:2n-6)	30.0	2.8	26.8-35.6	24.5	5.5	16.3-33.8	24.0	3.5	18.9-24.9	<0.001	0.143	<0.001
Di-homoγ-linolenic acid (20:3n-6)	1.7	0.6	1.3-2.5	1.3	0.4	0.7-2.4	1.5	0.6	1.3-2.2	0.002	0.057	0.762
Arachidonic acid (20:4n-6)	7.0	1.5	4.6-10.3	5.3	2.0	1.3-8.8	6.4	2.1	5.0-8.9	<0.001	0.045	0.672
α-linolenic acid (18:3n-3)	0.3	0.1	0.1-0.5	0.3	0.3	0.1-1.9	0.3	0.2	0.3-0.5	0.156	0.785	0.090
Eicosapentaenoic acid (20:5n-3)	0.3	0.2	0.1-0.5	0.3	0.2	0.1-3.6	0.5	0.3	0.3-1.0	0.632	0.020	0.007
Docosahexaenoic acid (22:6n-3)	1.6	0.5	1.1-2.3	0.9	0.7	0.2-2.8	1.4	0.2	0.9-2.6	<0.001	0.029	0.486

[a]Median of percentage weight.
[b]IQR=interquartile range.

(such as fish and hen's egg) and the elimination of such foods may have contributed to the plasma fatty acid profile observed at baseline. Because deficiency of polyunsaturated fatty acids may exert long-term functional effects on the brain and the cardiovascular and immune systems,[26-28] interventions aimed at improving the quality, rather than the quantity, of fat intake seems advisable in children with FA. In our study dietary counseling was able to increase the levels of polyunsaturated fatty acids, whereas it reduced the level of linoleic acid even further. Future studies are required to establish the nature of this finding.

To limit possible confounding variables affecting the results, all study participants were evaluated when they were in a stable clinical condition and after a median duration of exclusion diet of 10.8 months, which is sufficient to obtain disappearance of signs and symptoms of FA. Possible error in reporting dietary intake by the parents of children with FA or of control participants could not be excluded. However, there is no reason to expect that this error was different for healthy children and children with FA. Another limitation of our study is the lack of follow-up data on children without FA, and the lack of a control group of children with FA not receiving dietary counseling. For obvious ethical reasons it was not possible to evaluate patients with FA with inadequate energy intake and growth not receiving dietary counseling during a 6-month follow-up. However, previous studies in which children with FA were monitored frequently demonstrated the persistence of an impaired growth pattern,[4,29] suggesting that the results were mainly related to the effect of dietary counseling.

CONCLUSIONS

Our study demonstrates that suboptimal nutritional status is a frequent problem for children with FA and that dietary counseling, provided by a dietitian, is an effective strategy to promote rapid nutritional recovery in these children.

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STATEMENT OF POTENTIAL CONFLICT OF INTEREST

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