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The Effect of an Elimination Diet on Early Childhood Growth in Children with Egg and/or Cow's Milk Allergies

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ABSTRACT

Objective: Eliminating egg and/or cow's milk during early childhood may affect the growth of food-allergic children. The aim of this study was to determine the effects of elimination diets on anthropometric measurements and diet composition in children allergic to egg and/or cow's milk.

Materials and Methods: Anthropometric measurements and nutritional data were evaluated in children with cow's milk and/or egg protein allergy during elimination diets. Their daily calorie, carbohydrate, fat, and protein intakes were analyzed based on a 3-day diet log. Z-scores for weight, height, weight-for-age, and weight-for-height were calculated. The data were compared with pre-elimination values and with those of healthy controls.

Results: The study included 77 food-allergic children and a control group of 50 healthy children. In the patient group, the median age was 14 months and 57.1% (n=44) were male. Age, gender, and z-scores for weight-for-age and height-for-age were similar between the groups. Comparisons with pre-elimination measurements revealed that 18.2% of children with short stature at the time of diagnosis achieved normal height after elimination diets (p=0.001) and 37.4% of the children had increased height z-score. However, weight-for-age z-score decreased significantly (p<0.01). Although caloric intake was the same in both groups, the patient group consumed relatively less protein and more fat and carbohydrates.

Conclusion: In elimination diets, even if the calorie intake is adequate, eliminating allergenic food items may cause a decrease in weight without causing malnutrition. The height may improve. Growth should be monitored with age-corrected measurements and on an individual basis.

Keywords: Anthropometric measurements, cows' milk allergy, egg allergy, elimination diets, food allergy

INTRODUCTION

There has been an increase in the incidence of food allergies (FA), which is an important disease that especially affects young infants and children. The prevalence is estimated to be as high as 10% in children (1). Cow's milk and egg are the two most common causes of FAs in children (2,3). There is no cure for FA; the treatment approach involves symptom management and allergen avoidance (4). Several previous studies have shown that eliminating allergens from the diet may pose a risk for nutritional deficiencies and growth impairment (5-7).

Eliminating foods that contain cow's milk and egg may cause an imbalance in children's dietary macronutrient (proteins, fat, carbohydrates) distribution (5,7) and impact growth (6). Therefore, monitoring the nutritional status of children and providing nutritional support are crucial (5-9).

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The aim of this study was to evaluate the anthropometric measurements (AMs), caloric intake, and dietary composition of children with cows' milk and/or egg protein allergy while on restricted diets compared to those of healthy peers and their own pre-elimination data.

MATERIAL and METHODS

This cross-sectional study was performed at the pediatric allergy department of Ankara Children's Health and Disease Hematology Oncology Hospital between July 2012 and July 2015. The local ethics committee approved the study design (protocol number: 20.06.2012/26). Verbal consent to participate in the study was obtained from the patients' parents.

Study Population

Patient group: Children 0–36 months of age who were diagnosed as having cow's milk and/or egg allergy were included in the patient group. Those with non-allergic comorbidities (e.g., cerebral palsy, heart disease, extreme prematurity) were excluded.

Control group: Healthy children aged 0–36 months who were followed up at the department of social pediatrics of our hospital were included in the control group.

Children in the patient group were evaluated with specific allergy tests, whereas those in the control group were not subjected to any allergy testing. In both groups, height and weight were measured and the parents were asked to keep a detailed diet-log for 3 days.

Allergy Workup

Diagnosis of FA was based on the clinical history and laboratory tests (specific-IgE, skin prick test [SPT]) and/or food challenge tests, in accordance with the relevant guidelines (10, 11). SPT was performed to detect IgE-mediated sensitization using commercially available solutions (ALK-Albelló, Madrid-Spain) of cow's milk, egg, soy, and peanut (the most common food allergens in early childhood) (2,3). SPT reactions were evaluated according to induration (wheal) size and compared with the positive control. Wheals larger than 3 mm in diameter were evaluated as positive. A negative SPT confirmed non-IgE mediated reactions.

Food-specific IgE (sIgE) antibodies were investigated from the patients' serum samples using the immunoCAP (Phadia-AB, Uppsala, Sweden)/immunolight (Siemens Healthcare Diagnostics, Tarrytown, NY, USA) test. Serum sIgE concentrations higher than 0.35 kU/L were considered positive in the determination of IgE-mediated reactions.

Oral food challenge (OFC) was also performed in patients with suspected single FA according to guideline recommendations based on the patient's age and reaction (e.g., patients with anaphylaxis history did not undergo oral challenge) (11,12).

Furthermore, an elimination diet excluding the suspected food was administered for 15–30 days for diagnostic purposes and the clinical improvement was evaluated. Recurrence of symptoms upon reintroduction of eliminated foods was regarded as confirmation of allergy to those foods.

Three-Day Diet Log

All children diagnosed as having FA were referred to a dietitian for nutritional counseling. To assess the children's dietary intake, their parents were asked to keep a detailed dietary log for 3 days. This log was recorded at least 8 weeks after initiating the elimination diets and was timed to include 2 weekdays and 1 weekend day. The parents recorded meal contents and portion sizes. The data in the dietary logs were analyzed by the dietitian using the Turkish version of the Nutrition Database Program (NDBP) (13). Fat, protein, carbohydrate and calories were calculated separately from the NDBP and evaluated according to the guideline recommendations for healthy children (14,15).

Anthropometry

Pre-elimination weight and height measurements were obtained from the clinical files. Post-elimination weight and height measurements were recorded at least 3 months after initiation of the elimination diet. Control group measurements were recorded during routine well-child visits.

Weight was measured using the same portable electronic baby (<10 kg) or sitting (>10 kg) scales, which were calibrated as per hospital protocol. Height was measured using a portable recumbent infantometer for children under 2 years of age, and a fixed standing stadiometer for older children (rounded to the nearest 0.1cm). Z-scores were used to standardize measurements to age and gender. We evaluated z-scores of <-2 as low, -2 to 2 as normal, and >2 as high. Z-scores were calculated for all growth measurements using the WHO standards and percentile scales, which were adapted to Turkish children (15-17).

Change in z-score was calculated for the food-allergic children's AMs obtained before and after elimination. Weight-for-age and weight-for-height values were calculated using sex-specific standard scales.

Statistical Analysis

Statistical analyses were performed using the IBM SPSS Statistics for Windows version 22.0 (IBM Corp., Armonk, NY, USA) software. Numbers and percentages were reported for discrete variables. Continuous variables were summarized using mean and standard deviations for normally distributed data and as median and interquartile range (IQR) for non-normally distributed data. The chi-square ($\chi 2$) test was used to compare nonparametric data; the Mann–Whitney U test was used for comparisons of non-normally distributed continuous variables and the independent-samples t-test for normally distributed continuous variables. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 127 children (77 allergic and 50 healthy) were included. The median age (IQR) of the food-allergic children was 14 (6–35) months and 44 (57.1%) were male. There were no statistically significant differences in sex or age between the groups. The demographic features of the groups and FA distribution were presented in Table I.

Table I: Characteristics of patients and controls.

	Patient	Control	p
Age (months), median (IQR)	14 (6-35)	13 (4-36)	0.917
Gender, n (%) Boy/Girl	44 (57.1) / 33 (42.9)	25 (50) / 25 (50)	0.430
Gestational age, n (%) Term/Preterm	68 (88.3) / 9 (11.7)	45 (90) / 5 (10)	0.995
Type of delivery, n (%) Cesarean / Normal vaginal route	44 (57.1) / 33 (42.9)	26 (52) / 24(48)	0.408
Weight at birth, median (IQR)	3260 (1470-4500)	3300 (1060-4260)	0.720
Height at birth, median (IQR)	50 (43-55)	50 (40-55)	0.475
Duration of breastfeeding, median (IQR)	10 (0-28)	12 (0-26)	0.402
Starting age of supplementary food, median (IQR)	6 (4.5-6)	6 (5.5-6)	0.636
Age at symptom onset (months) (IQR)	3 (1-12)		
Age at diagnosis (months) (IQR)	5 (1-12)		
Allergy, n (%)			
Cow's milk	18 (23.4)		
Egg	27 (35)		
Cow's milk+egg	32 (41.6)		
Types of reactions, n (%)			
IgE	69 (89.7)		
Non-IgE	8 (10.3)		
Duration of elimination diets (months), mean±SD			
Cow's milk	11.5±7.5		
Egg	10±7.3		
Symptoms			
Dermatologic, n (%)	66 (5.7)		
Gastrointestinal, n (%)	28 (36.4)		
Respiratory, n (%)	14 (18.2)		
Total IgE (kIU/L), median, (IQR)	41.5 (9-291.5)		
Eosinophil (%), median (IQR)	4 (2-8)		

IQR: Interquartile range

Anthropometric Measurements

Comparison of allergic children's post-elimination measurements with healthy peers

The cross-sectional values of the patients' weight, height, weight-for-age, and weight-for-height after at least 3 months of elimination were similar to those of healthy peers (p=0.636, p=0.997, p=0.288, p=0.584) (Table II).

Comparison of allergic children's pre- and post-elimination measurements

The cross-sectional z-scores for weight and weight-for-height in patients after at least 3 months of elimination were similar to those of their pre-elimination measurements (p=0.71, p=0.094). However, median z-score for height increased significantly after elimination (p=0.00) and the median weight-for-age also decreased significantly during same period (p=0.001) (Table III).

Four (5.2%) of the underweight food-allergic children achieved normal weight, but the difference was not statistically significant. After elimination, 18.2% of children with short stature at the start of the elimination diet achieved normal height (p=0.001), while 37.4% (n=29) of the children showed increases in z-score for height (Figure 1A-D).

Dietary Intake Analyses

There was no statistical difference in daily caloric intake between the allergic and control groups (644 kg/cal and 672 kg/cal, respectively; p=0.741). Percentage of protein consumption was higher in the control group than in the allergic group (p<0.01), whereas consumption of fat (p<0.001) and carbohydrates (p=0.004) was higher in the allergic group. Fat, carbohydrate, and protein consumption values were calculated separately as grams and percentages for both groups (Table IV).

Table II: Comparison of the post-elimination Z-scores for anthropometric measurements for the patient and the control groups.

Measurements	Patient	Control	p
Z-score for weight, median (IQR)	0.13 (-0.58, 0.92)	0.18 (-0.82, 0.93)	0.636
Z-score for height, median (IQR)	0.27 (-0.58, 1.25)	0.25 (-1.23, 1.09)	0.487
Z-score for weight-for-age, median (IQR)	-0.15 (-1.02, 0.38)	0.06 (-0.66, 1.08)	0.288
Z-score for weight-for-height, median (IQR)	-0.09 (-0.58, 0.80)	0.06 (-0.65, 0.93)	0.584

IQR: Interquartile range (25th percentile, 75th percentile)

Table III: Z-scores for pre- and post-elimination anthropometric measurements of the patients.

Measurements	Pre	Post	p
Z-score for weight, median (IQR)	-0.02 (-0.87, 0.81)	0.01 (-0.63, 1.00)	0.710
Z-score for height, median (IQR)	-0.21 (-1.29, 0.79)	0.27 (-0.58, 1.26)	0.000
Z-score for weight-for-age, median (IQR)	0.38 (-0.65, 1.45)	-0.60 (-0.66, 1.08)	0.001
Z-score for weight-for-height, median (IQR)	0.29 (-0.87, 1.13)	0.06 (-0.65, 0.93)	0.094

IQR: Interquartile range (25th percentile, 75th percentile)

Table IV: Composition and calories of the diets of the patient and the control groups.

	Patient	Control	p
Calories (IQR)	672 (482-841)	644 (475-827)	0.74
Protein (gr) (IQR)	19.3 (11.4-28.7)	31.5 (18.8-40.5)	<0.001
Protein % (IQR)	12 (10-14)	41(17-47)	<0.001
Fat (gr) (IQR)	31 (20-46.3)	25.4 (16-33.4)	0.030
Fat % (IQR)	42 (35-48)	17(14-37)	<0.001
Carbohydrate (gr) (IQR)	65.9 (44.7-88.5)	59.95 (45-91.8)	0.677
Carbohydrate % (IQR)	44 (38-51)	40(35-45)	0.004

IQR: Inter Quartile Ranges

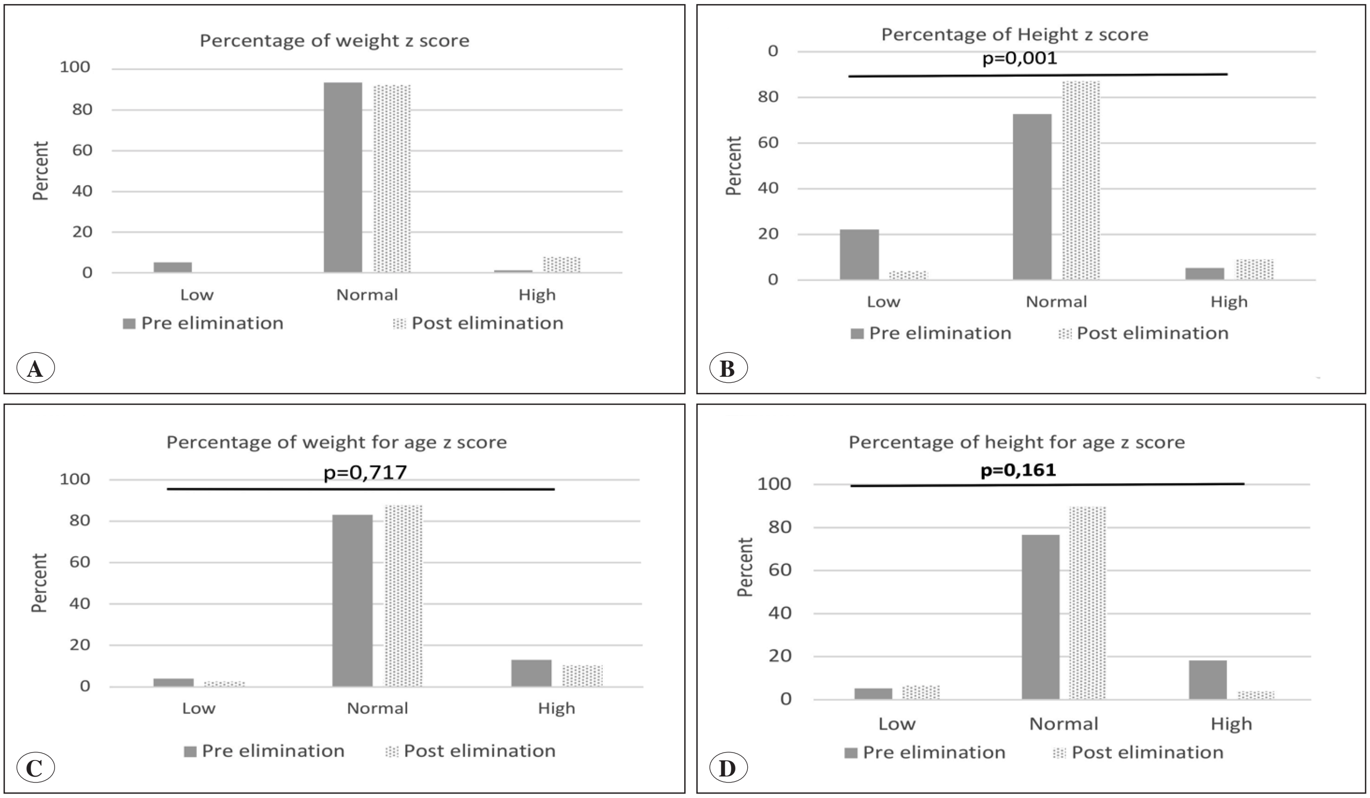

Figure 1. Distributions of the Z-scores for anthropometric measurements of the patients for **(A)** weight, **(B)** height, **(C)** weight-for-age, and **(D)** weight-for-height before and after elimination diets. Z-scores <-2 were interpreted as low, -2–2 as normal, and >2 as high.

Comparison of post-elimination measurements and dietary compositions of children with only milk allergies to with children with only egg allergies.

The values of the patients' who had only milk allergies for weight, height, weight-for-age, and weight-for-height after at least 3 months of elimination were similar to those of only egg allergic peers (p= 0.661, p=0.893 p=0.787, p=0.884). There was no statistical difference in daily caloric intake and percentage of protein consumption between groups (respectively p=0.418, p=0.979). However, the percentage of fat consumption was higher in the egg allergic group than in the milk allergic group (p=0.002), whereas consumption of carbonhydrates was higher in the milk allergic group (Table V).

Comparison of post-elimination measurements and dietary composition of children with only milk or egg allergies (single food allergy) with children with both milk and egg allergies (multiple food allergies).

The values of the patients with single food allergies (milk or egg) including weight, height, weight-for-age, and weight-for-height after at least 3 months of elimination were similar to those of multiple allergic peers (p=0.705, p=0.116, p=0.778, p=0.131) (Table V). Daily calorie intake and the percentage of fat and protein consumption were similar in both groups (respectively p=0.971, 0.138, 0.979). However, the percentage of carbohydrate consumption was a little bit higher in the multiple food allergic children (47%) than in single food allergic ones (44%) (p=0.028).

DISCUSSION

In our study, we found that there were no statistically significant differences in anthropometric z-scores and caloric intake between food-allergic children on elimination diets and healthy controls, but there were differences in dietary fat, carbohydrate, and protein composition. In addition, although elimination diets resulted in improved stature in food-allergic children compared to pre-elimination measurements, there was a decrease in weight-for-age that was more pronounced in children with multiple FAs.

Infancy is a period of rapid growth, and various previous studies have shown that eliminating basic nutritional sources such as milk and eggs in childhood

Table V: the difference of anthropometric measurements and dietary intakes according to egg & milk allergies.

Parameters	Milk allergy n=18	Egg allergy n=27	P	Single food allergies (egg/milk) n=45	Multiple food allergies (egg&milk) n=32	P
The changes of weight z-scores Median (IQR)	0.14 (-0.6-0.82)	0.14 (-0.77--1.11)	0.661	0.14 (-0.62-1.13)	0.25 (-0.30-0.89)	0.705
The changes of height z-scores Median (IQR)	0.58 (-1.58-0.82)	0.63 (-0.46-1.78)	0.893	0.59 (-0.56-1.46)	1.01 (-0.47-2.6)	0.116
The changes of weigh for ages z-scores Median (IQR)	-0.44 (-1.5-0.82)	-0.46 (-1.38-0.23)	0.787	-0.45 (-1.45-0.40)	-0.60 (-1.33-0.95)	0.778
The changes of weight for height z-scores Median (IQR)	-0.70 (-1.5-1.49)	0.12 (-1.66-1.36)	0.884	0.01 (-1.54-1.40)	-0.75 (-1.84-0.73)	0.131
Calories (kcal) Median (IQR)	592 (367-891)	737 (443-937)	0.418	656 (405-913)	694 (508-824)	0.971
Protein Median (IQR)						
Grams	20 (1.8-30)	17.4 (10.7-28)	0.620	17.9 (10-29)	20.7 (13-29)	0.775
%	13.5 (11-15)	12 (10-14)	0.257	12 (10-14)	13 (10-25)	0.979
Fat Median (IQR)						
Grams	21.9 (17.4-37.1)	45.9 (24.8-57.1)	**0.006**	32.8 (20-50)	29.7 (18-39)	0.136
%	37.5 (35-43)	45.5 (41.2-54)	**0.002**	43 (36-50)	38 (30-47)	0.138
Carbohydrates Median(IQR)						
Grams	56.5 (35.7-118)	61.5 (39-85)	0.982	61.5 (38-89)	80 (59-92)	0.177
%	45.5 (43.7-51.8)	38 (35-46)	**0.005**	44 (35-48)	47 (41-57)	**0.028**

IQR: Interquartile range

can affect normal growth (18,19). Tiainen et al. (18) compared AMs in children on an elimination diet due to milk allergy and healthy children and found that although both groups had similar caloric intake, the allergic group had lower height-for-age. Similarly, Mehta et al. (20) have observed that food-allergic children who had one or more foods eliminated from their diet were shorter and weaker than healthy controls and their growth was significantly affected. In contrast, Rowicka et al. (19) have found no statistical differences in height, weight, or BMI between healthy children and children with cow's milk protein elimination. In our study, we found no statistically significant differences between the AMs of food-allergic children on a milk and/or egg elimination diet and healthy controls. One reason for this may be early diagnosis due to easy access to healthcare in Turkey, because all children under the age of 18 have social health insurance. Another reason may be that all patients were under nutritional follow-up by a dietitian.

We compared food-allergic patients' pre- and post-elimination AMs. A child with a normal percentile and z-score relative to her/his peers may actually be growing better or worse according to their potential. Paganus et al. (21) found that milk-allergic children who initially had short stature were still short and also lost weight while on a milk elimination diet. A study by Meyer et al. (9) showed that with appropriate dietary counseling, growth parameters increased between pre- to post-elimination. When we assessed food-allergic children's post-elimination AMs compared to pre-elimination values, we observed improvement in z-scores for stature but a decrease in weight-for-age, while no significant change was seen in weight or weight-for-height. Weight loss may reflect disease activity in systemic diseases before it impacting vertical growth (22). Height is affected by disease and nutrition in the long term. In our study, the duration of elimination diet was 8 months, but during this period the patients' caloric intake may have fluctuated due to disease activity or other reasons such as infections or tooth eruptions. Therefore, this finding may be the result of acute events, as weight-for-height z-scores were unchanged and height z-scores increased. A limitation of our study was that our analysis of dietary logs was cross-sectional, and we had no data regarding the patients' daily calories or dietary composition before the elimination diets.

Our finding that z-scores for weight remained unchanged while z-scores for weight-for-age decreased during elimination diets indicates that height and weight measurements alone are inadequate for the growth assessment of rapidly growing children. Height- and weight-for-age are necessary for correct interpretation of growth (23) because, as seen in our study, patients did not lose weight but also did not gain weight as they should have. This resulted in unchanged weight z-scores while weight-for-age z-scores decreased.

There may be several explanations for the increase in height z-scores after elimination diet in this study. One is that FA leads to disruption of the mucosal barrier and absorption, leading to intestinal inflammation. Even if nutritional support is provided, if allergen exposure continues, the intestinal barrier will not heal, leading to reduced absorption of various vitamins, minerals, and major nutrients (24). However, removing the allergen through the elimination diet may have reduced symptoms, increased mucosal healing, and triggered tolerance, thereby leading to enhanced growth.

Another possible reason is that the stress caused by inflammation and barrier dysfunction may increase levels of cytokines in the body, which can affect the growth of children. An experimental animal model by Koniaris et al. (25) showed that intestinal inflammation affects linear bone growth independent of diet because cytokines may suppress bone growth. Also, removing the allergen from the diet may reduce stress in the body and alter the balance of intestinal cytokines. Several studies have provided evidence that cytokines impact vertical growth (24). This link should be explored with new studies. We did not investigate this in our study, but our results did support the literature showing that FA affects growth (5-7), as the allergic children in our study were shorter according to z-score at diagnosis and before treatment, and showed improvement in height z-scores after starting the elimination diet.

Our analyses showed that food-allergic children on cow's milk and/or egg elimination diets and healthy children consumed similar calories, but the content of their diets differed. It is important to provide the calories needed by the child when performing an elimination diet due to FAs like egg and cow's milk. Removing the basic protein sources of early childhood, such as milk and eggs, can lead to changes in the caloric intake and nutrient distribution. For example, Tiainen et al. (18) have analyzed 6-day dietary logs of 18 healthy children and 20 children with milk allergy and detected no difference between the groups in terms of caloric intake. However, the milk allergy group had relatively lower protein intake and higher fat consumption. Henriksen et al. (26) examined the cow's milk elimination diets of patients under 2 years of age and found that they received less energy, fat, protein, calcium, niacin, and riboflavin than children fed cow's milk.

Similarly, in our study the caloric intake was similar in both groups, while the food-allergic children on elimination diets consumed less protein but more fat and carbohydrates then their healthy peers. It should be noted that although the food-allergic children consumed more fat and carbohydrates, they did not exceed the recommended values for a healthy child (14,15). In addition, egg allergic children consumed more fat but less carbohydrate according to milk allergic peers in our study where as calorie intake and protein consumptions were similar in both groups. Moreover, calorie intakes and percentage of fat and protein consumption were similar in multiple and single food allergic children. However, the percentage of carbohydrate consumption was higher in multiple food allergic (both egg and milk) children than in single food allergic (milk or egg) children. Although the types and numbers of allergen foods affect the compositions of diets; there was also no statistically significant difference in all anthropometric measurement changes in our study. Previously, the effect of a milk elimination diet on the growth of children has been shown in various studies (5-9). Although we had a low number of patients, we have shown that egg elimination alone also affects the growth of children.

Increased percentage of total calories from fat may be a reason for the increase in the height z-score after elimination in our patients. Adu-Afarwuah et al. (27) have found that fatty acid consumption was associated with increased height. In addition, Uauy et al. (22) reported that providing less than 22% of energy from fats reduced growth. In our study, when the initially shorter food-allergic children had restricted protein, they replaced it with fat (post-elimination diet was 42% fat). This may explain the improvement seen between pre- and post-elimination z-scores for height.

Although the food-allergic children consumed less protein and more fat and carbohydrates than their healthy peers, these differences in dietary composition were not above or below the European Society of Pediatric Gastroenterology, Hepatology and Nutrition's (ESPGHAN) recommendations for healthy children (15). Therefore, allergic children on elimination diets replaced protein deficits with fat and carbohydrates. Studies have demonstrated that growth failure in food-allergic children is associated with insufficient and poor diet, so dietitian consultations are important for better growth (20,28).

Our study demonstrated both positive and negative effects of food allergen elimination diet on growth, unlike most studies to date. A strong point of this study is that we compared patients both to themselves (pre- and post-elimination values) and to healthy controls. Limitations of our study are that it was a single-center study and we used only AMs to assess nutritional status and did not evaluate vitamin and/or mineral status. In addition, dietary counseling was provided only to patients and not to controls, which may have introduced bias.

In conclusion, eliminating allergenic foods during elimination diets may cause a decrease in weight without causing malnutrition even if the calorie intake is adequate. However, the appropriate elimination of food allergens with balanced replacement can improve stature, even if weight-for-age decreases. During physical examination in the clinic, weight-for-age should be evaluated in addition to height and weight for a better growth assessment. Total caloric intake is a major determinant of growth if fat, carbohydrates, and protein are balanced. Dietitian consultation and sufficient calorie intake are important for growth in food-allergic children.

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