

The Impact of Dietary Therapy on Clinical and Biologic Parameters of Pediatric Patients with Eosinophilic Esophagitis

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What is already known about this topic? Three dietary regimens have been shown to be effective in children diagnosed with eosinophilic esophagitis (EoE): the strict use of an amino-acid formula, dietary restriction based on eliminating the most likely food antigens, dietary restriction based on multimodality allergy testing.

What does this article add to our knowledge? In children with EoE, after 2 months of a dietary therapy that combined both types of elimination diet with an amino-acid formula as a replacement for dairy products, the nutritional status was mildly affected by EoE and not worsened by the 2-month dietary therapy.

How does this study impact current management guidelines? Dietary therapy with an amino-acid formula as a replacement for dairy products is nutritionally adapted to the treatment of EoE.

BACKGROUND: Eosinophilic esophagitis (EoE) is a clinicopathologic disease that presents with a massive infiltration of the esophagus by eosinophils triggered by food antigen(s). **OBJECTIVE:** To determine the impact of dietary therapy on nutritional parameters in patients who present with EoE. **METHODS:** A convenience retrospective study analyzed patients with EoE after a 2-month dietary therapy (6-food elimination diet, avoidance of the 6 most common allergenic foods, plus avoidance of those eliciting positive skin testing, plus

amino-acid formula as replacement for dairy products). Pre- and postdiet allergic and nutritional status were evaluated. **RESULTS:** Of 111 eligible patients, 59 patients, with a median age of 77.7 months (range, 9-189 months) were enrolled. Dietary therapy significantly increased the return to normal endoscopic appearance (47.4%, $P < .0009$) and led to complete remission (<5 eosinophils/esophageal HPF and disappearance of symptoms) in 59.3%. All symptoms improved, digestive (98.3%), cutaneous (80%), and respiratory (92.8%). The prediet median weight-for-height (WFH) z score was -0.75 (-3.00 to 5.69), and the postdiet WFH did not significantly differ, -0.51 (-3.09 to 5.00). The prediet WFH z score was less than -2 (moderate malnutrition) in 10.1%. Postdiet blood eosinophils counts decreased in absolute numbers and in counts $\geq 500 \times 10^6/L$ ($P < .0001$). Evaluation after 1 year of progressive reintroduction of eliminated foods was available in 33 children: the median WFH z score did not significantly improve, from -0.89 (range, -3.00 to 0.67) at enrollment to -0.59 (range, -3.66 to 2.24).

CONCLUSION: The nutritional status of children with EoE was mildly affected and not worsened by the 2-month dietary therapy. © 2014 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2014;2:587-93)

Key Words: Eosinophilic esophagitis; Dietary therapy; Nutritional status

Eosinophilic esophagitis (EoE) is a clinicopathologic disease characterized by an eosinophilic infiltration of the esophagus,¹⁻³ driven by allergic and genetic factors.³⁻⁵ A food elimination diet is effective in children.^{6,7} The updated consensus on EoE management recommends 3 dietary methods: an “elemental” diet, which removes all foods, with an amino acid-based formula (AAF) as a substitute; a diet that eliminates the most likely food

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Conflicts of interest: C. Dupont is on the Nutricia Baby Nutrition Board, the Nestlé Clinical Nutrition Board, and is chairman of the DBV Technologies Scientific Advisory Board; has received consultancy fees from Sodilac, France; has received lecture fees from Danone Baby Nutrition, Nestlé, Mead-Johnson, Pfizer, and United Pharmaceuticals; has patents with DBV Technologies, Nutricia, and Paris Descartes University and Assistance Publique Hopitaux de Paris; and has stock/stock options in DBV Technologies. F. Campeotto receives royalties from Mead Johnson. D. Colson has received research support from and is employed by Nutricia Nutrition Clinique, Saint Ouen, France. The rest of the authors declare that they have no relevant conflicts of interest.

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Abbreviations used

AAF- Amino-acid formula
 APT- Atopy patch test
 EGD- Esophagogastroduodenoscopy
 EoE- Eosinophilic esophagitis
 HFA- Height for age
 HPF- High-power field
 IQR- Interquartile range
 ns- not significant
 SFED- Six food elimination diet
 SPT- Skin prick test
 WFH- Weight for height

antigens, cow's milk protein, wheat, soy, egg, peanut, nuts, and fish and/or seafood,⁸ namely the 6 food elimination diet (SFED); and an elimination diet based on multimodality allergy testing. Histologic remission was better with the elemental diet than with the SFED or the skin prick test (SPT) directed diet.⁹ These regimens involve a severe dietary restriction³ in children (some with existing feeding difficulties). They may represent a nutritional risk, especially for growth.¹⁰⁻¹² Studies on the elimination diets focused on the allergic outcome of the disease, that is, esophageal eosinophilic infiltration and clinical symptoms,^{6,7,13} rather than on their safety and/or tolerance. Also, the nutritional status of children with EoE has yet to be investigated.

Patients with EoE who are referred to our pediatric gastroenterology tertiary reference center are offered a standardized dietary therapy, the so-called modified SFED,⁹ in which avoidance comprises the 6 most common allergenic foods and those detected through directed SPTs and atopy patch tests (APT); an AAF is prescribed as a replacement for dairy products. In line with the recommendations from consensus groups,¹⁻³ we took advantage of this standardized treatment to analyze retrospectively its clinical, especially nutritional, and biologic outcomes.

METHODS**Study design**

This retrospective convenience cohort study enrolled all children with EoE successively referred to the pediatric gastroenterology department of Hospital Necker-Enfants Malades. Participants were recruited from the Allergie Recherche Serum Nourrissons & Enfants (ARSENE) cohort, a collection of blood and biopsy samples registered within the French Ministry of Health (DC-2009-955). Written informed consent was obtained from all the parents and from children 11 years old and older.

Subjects

After the diagnosis of EoE, the first clinical and biologic assessment allowed the same physician to check the nutritional and allergic status of the child. After a 2-month dietary therapy, a second esophagogastroduodenoscopy (EGD), as recommended,³ checked the efficacy of the diet, and a second clinical and biologic assessment detected any need for additional treatment and guided the progressive reintroduction of the potentially offending foods.³ All consecutive records were reviewed, and the patients were considered eligible (Figure 1) if they had ≥ 15 eosinophils/HPF in at least 1 esophageal biopsy,^{1,3} no association with another eosinophilic condition and no response to a proton-pump inhibitor ≥ 1 mg/kg/d for at least 4 weeks and/or normal pH probe tracing. Enrollment criteria were EGD and nutritional

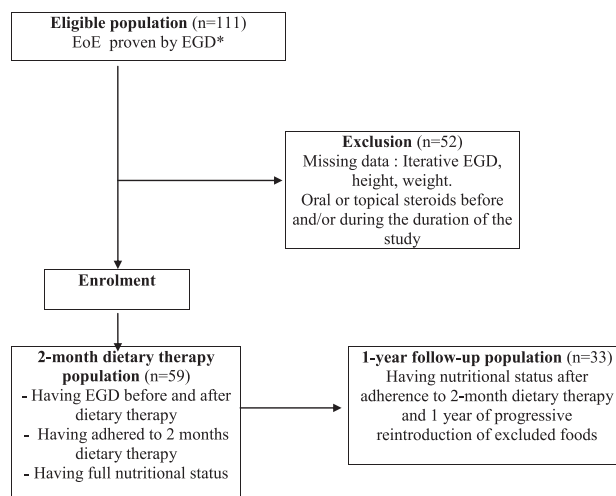


FIGURE 1. Flow chart of enrolled children according to entry criteria and to adherence of patients to dietary therapy. Eligible children were enrolled in the 2-month dietary therapy population if they had EGD and nutritional status available before and after a 2-month dietary therapy. The 1-year follow-up population consisted of patients from the latter group for whom nutritional status also was available after 1 year of progressive reintroduction of foods.

status available before and after a 2-month dietary therapy and no oral or topical glucocorticoids. The enrolled patients constituted the “2-month dietary therapy” population. The “1-year follow-up” population consisted of patients from the latter group for whom nutritional status also was available after 1 year of progressive reintroduction of foods.³ Asthma medications and medications that do not affect esophageal eosinophils were permitted. Atopy was considered if patients had asthma, allergic rhinitis, or atopic dermatitis and a positive SPT.

Dietary therapy

The modified SFED combined SFED with the elimination of the foods that elicited a positive SPT and/or APT. These tests were performed routinely for milk, egg, wheat, and soy and, according to a previous clinical reaction, to one or more other specific food(s).⁹ An AAF was prescribed as a replacement for dairy products, Neocate (SHS International, Nutricia, Liverpool, UK) or Nutramigen AA (Mead Johnson, Evansville, Ind) in infants, Neocate Advance (SHS International) in 1- to 10-year-old children, and Elemental (SHS International) in older children. The recommended daily consumption of AAF was 500 mL or more, based on the French pediatric feeding guidelines, which accounted for $\geq 30\%$ of total caloric intake. The 2-month dietary therapy started only when social security reimbursement was received for the AAF, that is, 2 to 3 months after the first assessment. A detailed explanation of the dietary therapy and its rationale was given. The parents could contact the nurse via mail or a dedicated telephone number to ensure nutritional balance. At the end of the 2-month period, the families reported whether or not the child had followed the diet. We verified that non-adherence was not related to feeding difficulties. Children were then prescribed a progressive reintroduction of eliminated foods, 1 every 3 months, starting with foods for which they had tested negative, before offering staple foods per patients' requests, AAF

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