Eosinophilic Esophagitis: Personalized Treatment With an Elimination Diet Based on IgE Levels in Children Aged <16 Years

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The treatment of eosinophilic esophagitis (EoE) using a food elimination diet (FED) is similar in children and adults [1], although it is not easy for the physician to choose the best therapeutic diet in patients aged <16 years.

FED produces a remission rate of 48% [2]. In children, an empirical food elimination diet (EFED) based on 4 or 6 foods induces a remission rate of >50% and >70%, respectively, although the former is less restrictive than the 6-EFED diet [3].

Rodríguez-Sánchez et al [4] performed a study with specific IgE-based elimination diets (sIgE-ED) (≥0.1 kU/L) and found a remission rate of 73% among adult patients with EoE [4]. This diet has not been studied in children under 16 years of age. Therefore, the objectives of the present study were to study the proportion of patients with EoE who respond (clinical and histological remission) to a FED based on sIgE (if ≥0.1 kU/L, sIgE-ED) to cow's milk, wheat, egg, lentils, peanuts, and hake/shrimp. We also determined the mean number of foods withdrawn and established which foods were most associated with the development of EoE, the number of patients who completed treatment with the reintroduction of the previously withdrawn food, and the number of endoscopies necessary for diagnosis and treatment of sIgE-ED.

This prospective, descriptive study examined a series of patients assessed in the EoE clinic during 2011-2016. Patients with esophageal dysfunction or swallowing disorders underwent esophagogastroduodenoscopy with biopsies (esophagus [2 in the upper, middle, and lower sections], stomach [2], and duodenum [2]). Patients were diagnosed with EoE if they had at least 15 eosinophils per HPF in the esophagus and no eosinophils in the stomach or in the duodenum.

After 6 weeks with sIgE-ED, patients again underwent esophageal endoscopy with biopsies. In the patients who responded (clinically and histologically), each food was reintroduced separately based on monitoring with endoscopy and biopsies 6 weeks after the introduction of a food and before introducing the next one.

All patients and/or their parents received written information about their sIgE-ED and were given a contact number and email address to clarify any doubts about the diet. Corticosteroids (oral and topical) were discontinued at least 8 weeks before starting the study and were the reason for exclusion from the study if they were necessary during this period. Patients who required treatment with bronchodilators such as $ß_2$-adrenergic agonists, anticholinergics, and antihistamines were not excluded from the study.

EoE remitted in 17 of 22 patients (Table). In the case of treatment with sIgE-ED, we withdrew 4 food families. The mean number of endoscopies was 5. Fifteen patients completed the reintroduction of food, with cow's milk being the food most involved, followed by nuts and fish.

Food can trigger EoE. The mechanism by which it initiates or facilitates eosinophilic inflammation needs to be further investigated, although it appears to be IgE-independent [5]. We based this study on sIgE-ED [4] in patients <16 years of age with EoE for a number of reasons. First, we thought that the results would be at least similar to those observed with adults. We indicated the sIgE-ED diet for a number of reasons. Second, EoE is a classic atopic disease, as it shares features with other atopic diseases (pathogenesis, genetics, epidemiology, and treatment options) [6]. Third, in patients with an allergic disease, such as local rhinitis, allergy tests would have yielded negative results [7], both in blood sIgE levels and skin tests with allergens. Fourth, some nonallergic conditions, such as chronic urticaria, respond to treatment with omalizumab (anti-IgE), sometimes even better than in cases of IgE-mediated asthma [8]. Fifth, IgE has been reported in the esophageal mucosa, although recent research indicates that the pathogenesis of EoE differs from that of IgE-mediated food allergy; in addition, levels of IgE (foods) in pediatric EoE are probably lower than in children with IgE-mediated allergy [9].

Therefore, we have established the cut-off point at ≥0.1 kU/L. Food-specific IgE levels indicate sensitization that may be clinical or subclinical. Generally, the higher the levels of IgE for a given food, the more likely it is that the patient has a clinical allergy to that food. Detection of specific IgE (ImmunCAP) to a food has been validated for immediate IgE-mediated hypersensitivity [10] but not for other types of hypersensitivity, such as delayed-type hypersensitivity.

With sIgE-ED, we were able to withdraw fewer foods, and the mean number of endoscopies was lower than if the patients had undertaken a 6-EFED. The foods withdrawn would have been similar with a 4-EFED, although the proportion of remissions would have been lower (64%). Our findings are in line with those of Kagalwalla et al [3], namely, cow's milk is the food most involved; however, our findings differ for the second and third most common foods involved. Fifteen patients were able to reintroduce the food, probably because the number of foods withdrawn was lower. As in adult patients, cow's milk was the food most involved in the development of EoE [4], followed by nuts and fish; however, the foods we identified as the second and third most common differed from those reported by other authors. With the sIgE-ED, our results are very similar to those obtained in adults with sIgE-ED,

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Table. Characteristics of Patients Undergoing a Specific IgE–Based Food Elimination diet

Patient	Age, y	Sex	Comorbidities	IgE, kU/L	Foods Withdrawn	Foods Reintroduced	Remission/ No Remission	Triggering Foods
1	10	M	RC, Aa (pollens)	W-0.8 M-0.5 P-0.3	C M N	C M N	R	M
2	5	M	RC, NAA	W-0.2 M-3.6 L-0.8	C M LG	C M LG	R	M
3	6	M	DA, NAA FA (E, PR)	M-0.3, E-2.1, P-0.8, L-1.8 W-1.1, PR-3	M, E, N, LG, C	M, CE, N, LG, C	R	M
4	9	M	RC (pollens) FA (M), AD, NAA (RV)	M-0.3, W-0.5 L-1.5, P-0.5 E-0.4	M, C LG, N, E	-	NR	-
5	11	M	FA (M, E)	M-3, E-1.2 W-0.2	M. E, C	-	NR	-
6	6	M	FA (E), CD RC (pollens)	M-1.6, E-0.4 F-0.1, W-0.2	M, E, F, C	M -	R	M
7	12	M	RC, A (pollen, FA (kiwi, LTP)	M-04, E-0.2, W-4.5, LG-2.7 P-7, F/PR 0.2	M, E, C, LG, N, F/PR	M, E, C, LG, N, F/PR	R	M, N
8	9	M	LI, nephrotic syndrome	M-2, E-0.5 W-0.1	M, E, C	-	NR	-
9	8	M	FA (nuts, LTP) LI, AD	P-9.5, W-2.5 L-5.4, E-0.2	C, LG, E	-	NR	-
10	15	M	RC, Aa (polysensitization) FA	M-1.6, W-16 E-1, L-5, P-22 H/P-29/21	M, E, C, LG, N, F/PR	M, E, C, LG, N, F/PR	NR	-
11	12	M	FA (E, LTP) AD, RC, Aa (pollens, molds)	M-0.6, W-0.9 L-0.5, P-0.6	M, C, LG, N	M, C, LG, N	R	M
12	15	M	AD	M-0.3	M,	M,	R	M
13	12	M	AD, OIT (M)	M-52, W-1, E-0.2, L-0.1, P-0.1	M, C, E, LG, N	C, E, L, N	R	M
14	11	M	RC, A (pollens)	M-0.6, W-2.2, L-0.9, P-0.8	M, C, LG, N	M, C, LG, N	R	M, N
15	7	M	FA (prawns)	M-1, W-0.8, E-0.3, L-0.2 H-0.9, P- 49	M, C, E, LG F/PR P	M - -	R	M
16	10	M	RC, Aa (pollens, molds)	M-0.3, E-6, W-0.8, L-0.3, P-1.3, H-0.5	M, E, C, LG, N F/PR	M, E, C, LG, N, F/PR	R	N
17	8	M	FA (some F and Lg)	M-0.2, E-0.4, W-0.4, L-,1, P-0.7, H-0.4	M, E, W, LG, N, F/PR	M, E, W, LG, N, F/PR	R	M
18	10	M	FA (E, Lg, N) RC, Aa (pollen, mushrooms)	M-0.9, E-0.6, W-0.2 L-1, P-1.2, H-0.5	M, E, W, LG N, F/PR	M, E, W, LG, N, F/PR	R	M, F/P
19	13	F	RC, Aa (pollen, molds) OIT (E)	M-0.8, E>100, W-0.9, L-0.2 P-0.3, H-0.5	M, E, W, LG, N, F/PR	M, E W, LG N, F/PR	R	M
20	13	M	RC, Aa (pollens)	M-1.1, W-0.6, P-0.2 H-0.1	M, W, N, F/PR	M, W, N, F/PR	R	M, N
21	12	M	RC, Aa (pollens, epithelia)	M-1.1, W-0.6, P-0.1, H-0.1	M, W, N, F/PR	M, W, N, F/PR	R	M
22	15	M	–	M-0.4	M	M	R	M

Abbreviations: Aa, Allergic asthma; AD, atopic dermatitis; C, cereals; CD, celiac disease; CE, cooked egg; E, egg; F/PR, fish/prawn; FA, food allergy; H, hake; L, lentil; Lg, legumes; LI, lactose intolerance; LTP, lipid transfer protein; M, milk; NAA, nonallergic asthma; N, nuts; OIT, oral immunotherapy; P, peanut; RC, rhinoconjunctivitis; RV, respiratory virus; W, wheat.

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although in this population, cereals and eggs follow cow's milk as the most common triggers of EoE [4].

It is sometimes difficult to undertake an FED, because if prepared foods are ingested, quantities of forbidden foods can be eaten without the patient being aware of it.

We believe that future studies similar to ours but with more patients are needed to confirm our results. The limitations of the study are discussed in the supplementary material.

We conclude that in EoE, any treatment involving an FED is valid, although we advise considering an sIgE-ED, since the number of endoscopies and foods withdrawn is lower, thus reducing the risk of immediate complications and improving patients' quality of life.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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