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A Single-Food Milk Elimination Diet Is Effective for Treatment of Eosinophilic Esophagitis in Children

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Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2021.03.049.

Conflicts of interest

This author discloses the following: Joshua B. Wechsler serves on the medical advisory board of the Campaign Urging Research for Eosinophilic Diseases. The remaining authors disclose no conflicts.

Abstract

BACKGROUND & AIMS: Cow's milk protein (CMP) is the most common trigger of inflammation in children and adults with eosinophilic esophagitis (EoE). We sought to assess the clinical, endoscopic, and histologic efficacy of dietary elimination of all CMP-containing foods in EoE.

METHODS: We performed a prospective observational study in children with EoE treated with the 1-food elimination diet (1FED), excluding all CMP. Children and their caretakers were educated by a registered dietitian regarding dietary elimination of all CMP-containing foods, with substitutions to meet nutritional needs for optimal growth and development, and daily meal planning. Upper endoscopy with biopsies was performed after 8 to 12 weeks of treatment. The primary end point was histologic remission, defined as fewer than 15 eosinophils per high-power field. Secondary end points were symptomatic, endoscopic, and quality-of-life (QOL) improvements.

RESULTS: Forty-one children (76% male; ages, 9 ± 4 years; 88% white) underwent 1FED education and post-treatment endoscopy with biopsies. Histologic remission occurred in 21 (51%) children, with a decrease in peak eosinophils per high-power field from a median of 50 (interquartile range, 35–70) to a median of 1 (interquartile range, 0–6; $P < .0001$). Endoscopic abnormalities improved in 24 (59%) patients, while symptoms improved in 25 (61%). Improved symptoms included chest pain, dysphagia, and pocketing/spitting out food. Parents perceived worse QOL, while children perceived improved QOL with the 1FED.

CONCLUSIONS: One-food elimination of CMP-containing foods from the diet induced histologic remission in more than 50% of children with EoE and led to significant improvement in symptoms and endoscopic abnormalities. The ease of implementation and adherence supports the 1FED as first-line dietary treatment.

Keywords

EoE; Treatment; Response; Dairy; Children; Dietary; Antigen

Eosinophilic esophagitis (EoE) is a chronic antigen-mediated allergic inflammatory disorder with significant treatment-associated impact on quality of life (QOL).[1] In a seminal publication, Kelly et al[2] established the role of food antigen(s) in triggering eosinophilia in EoE. Subsequent elemental diet as treatment studies showed remission in 88% to 95% of subjects.[3–5] An exclusive elemental diet is challenging to maintain, and requires numerous subsequent endoscopies to identify safe foods[6]; thus, less-restrictive diets are necessary. Kagalwalla et al[7] showed that a 6-food elimination diet (SFED) achieved remission in 75% of children with EoE, and similar response rates were shown in adults.[8,9] The superiority of a SFED over an allergy-test–directed elimination diet was shown by a meta-analysis.[10]

Despite high efficacy, adherence to a SFED can be challenging,[11] and there remains intense interest in less-restrictive dietary elimination strategies. Our group, in a prospective multicenter study, established the efficacy of a 4-food elimination diet (4FED) with histologic remission in 65% of children with EoE.[12] Even less restrictive 2-food group elimination diets are effective, but also can be difficult to implement and maintain.[13] We

and others have identified cow's milk protein (CMP) as the most commonly identified trigger of eosinophilia.[7,14–21] However, prior studies were limited by retrospective designs, small sample sizes, or age restrictions, and may not have estimated their efficacy accurately because of selection bias. Furthermore, CMP elimination studies have not used a histologic scoring system to assess inflammatory and structural changes, or addressed predictive factors of treatment response. Thus, studies to validate a 1-food elimination diet (1FED) of all CMP for EoE are necessary.

In this prospective study, we assessed the histologic, symptom, endoscopic, and quality-of-life outcomes in response to dietary elimination of all CMP in children with EoE. We also assessed predictive factors of treatment response.

Methods

Patient Recruitment

Patients ages 2 to 18 years with a previously confirmed diagnosis pf proton pump inhibitor (PPI)-refractory EoE per 2011 consensus guidelines[22] were recruited prospectively from gastroenterology clinics at the Ann and Robert H. Lurie Children's Hospital of Chicago from March 2012 to May 2017. Patients previously treated with swallowed steroids underwent a baseline endoscopy 3 months after discontinuing the medication to confirm recurrent esophageal eosinophilia (≥15 eosinophils per high-power field [eos/hpf]). Patients on PPI at study enrollment continued the medication once daily. Intranasal steroids for allergic rhinitis and inhaled steroids for asthma were continued. Patients on oral prednisone and those with non-EoE eosinophilic gastrointestinal disease, celiac disease, or inflammatory bowel disease were excluded from this study. The Institutional Review Board at the Ann and Robert H. Lurie Children's Hospital approved this study. Informed consent/assent was provided by the participants/their parents at the time of study enrollment.

Study Design

A 3-day pretreatment diet log was reviewed at enrollment to provide guidance about food substitution to ensure optimal growth. A single registered dietitian created standardized educational materials used for the duration of the study. Patients and parents were instructed on complete avoidance of all foods and supplements containing CMP. Meal planning used appropriate substitutions to meet the individual participant's nutritional needs. Food label reading was advised to avoid cross-contact. Printed instructions detailing specific guidance to avoid food contamination was provided to each family (Supplementary Tables 1–4). Avoidance of other animal milks such as goat or sheep was recommended, however, consumption of these milks (as cheese) was not noted on the 3-day pretreatment diet logs. Diet logs also were collected midway through the diet elimination to ensure compliance with food elimination and establish avoidance of contamination and, after review, the patient was cleared for follow-up endoscopy. Contamination or cross-contact with CMP resulted in delaying endoscopy for 4 weeks after removal of the contamination. Endoscopy therefore was performed 8 to 12 weeks after enrollment. The recruitment goal was 54 patients to power the study at 80%, with an a value of .05 for 51% of patients to have fewer than 15 eos/hpf.

Outcomes

The primary outcome was histologic response. Four samples each from the proximal, mid-, and distal esophagus were collected. H&E assessment of standard-of-care esophageal biopsy specimens was performed to determine the peak eosinophil count (PEC), defined as the maximal count of intra-epithelial eosinophils per high-powered field (0.23 mm^2). Patients with post-treatment biopsy specimens showing fewer than 15 or 15 or more eos/hpf were classified as 1FED responders or nonresponders, respectively.[23]

The secondary outcomes were improvements in symptoms, endoscopic findings, and QOL. Symptoms of esophageal dysfunction were collected at enrollment and post-treatment endoscopy. We used a 15-point scale that previously identified a response to 4FED.[12] This scale measures the presence or absence of the following: abdominal pain, chest pain, dysphagia, early satiety, feeding aversion, food impaction, gag, heartburn, odynophagia, pocket/spit out food, poor appetite, reflux/regurgitation, slow eating, and vomiting. Endoscopic features such as edema, rings, exudate, furrows, and stricture were scored as absent or present. PedsQL (Mapi Research Trust, Lyon, France) Generic and EoE-specific questionnaires were added before enrollment of the 24th patient. The questionnaires were collected for the following age groups: 5 to 7 years, 8 to 12 years, and 13 to 18 years. Further description of the PedsQL questionnaires is detailed in the Supplementary Methods section.

Statistics

Baseline dichotomous characteristics including demographics, symptoms, endoscopic abnormalities, atopy/comorbidities, concurrent medications, and allergy tests were summarized by frequency, and compared between histologic responders and nonresponders by the Fisher exact test (dichotomous variables) or the Student *t* test (continuous variables). Baseline and post-treatment PEC were summarized as the median (interquartile range [IQR]) and compared between histologic responders and nonresponders by the Wilcoxon rank-sum test. Changes before and after 1FED in PEC, EoE–histologic scoring system (HSS), symptom sum, endoscopic composites, and QOL scores were compared by the Wilcoxon signed-rank test. A binary logistic regression model was generated with treatment responder status as dependent and age at enrollment and carries EpiPen (Viatris, Canonburg, PA) as independent variables. Statistical analysis was performed using SAS/STAT version 9.4 (SAS Institute, Cary, NC) and R 3.5.3 (R Core team, Vienna, Austria).

Additional methods are described in the Supplemental Methods section of the Supplementary Materials.

Results

Patient Characteristics

Fifty-four patients were enrolled. Of these, 41 patients completed endoscopy 8 to 12 weeks after a 1FED (Figure 1). Seventy-five percent of these patients were male, with a mean age of 9 years (IQR, 6–13 y) (Table 1). Eighty-eight percent of patients were Caucasian with frequent personal or family histories of atopic diseases (Table 1). IgE-mediated food allergy

was present in 32% of patients; allergic rhinitis was the most common atopic comorbidity identified in 66% of patients and in 63% of family members. Sensitization to foods by skin prick tests was present in 65%, this was food-specific IgE in 78%. CM-specific IgE was present in 43%, skin prick test to CM was positive in only 11%. The median baseline eosinophil count was 50 eos/hpf (IQR, 35–80 eos/hpf) (Table 2). The baseline EoE-HSS grade/stage score was 9 (IQR, 8–12)/9 (IQR, 6–10) in the distal esophagus, 9 (IQR, 6–13)/9 (IQR, 5–11) in the midesophagus, and 7 (IQR, 3–11)/6 (IQR, 4–10) in the proximal esophagus (Table 2). A score of 9 defines mild-moderate severity because the maximum score is 21, whereas a score of 3 or less has been proposed as an EoE-HSS Remission Score.[24] Dysphagia (44%), early satiety (43%), slow eating (50%), and vomiting (34%) were the most frequent symptoms (Table 3). Endoscopic abnormalities were present, including edema and furrowing in 78%, exudates in 59%, and rings in 20% (Table 3), although no strictures were identified.

Change in Peak Eosinophil Count and Histology Scores

Of the 41 patients who underwent endoscopy after a 1FED, 21 (51%) achieved the primary histologic remission outcome of fewer than 15 eos/hpf (Figure 2A). Sixteen (39%) patients had 6 or fewer eos/hpf and 11 (27%) patients had 1 or fewer. We performed an intention-to-treat analysis by including all patients assessed for eligibility except those who withdrew or refused consent. By intention-to-treat analysis, 21 of 49 (43%) achieved histologic remission. The median PEC was reduced to 12 (IQR, 1–40; $P < .001$) (Table 2). The distal esophagus had the highest PEC and the proximal esophagus had the lowest after a 1FED (Table 2). A few histologic nonresponders had a decrease in eosinophilia in the proximal esophagus only (Figure 2B–D).

We found a significant reduction in the EoE-HSS grade and stage scores in the distal, mid-, and proximal esophagus after a 1FED (Table 2). There was a significant reduction in both the eosinophil and epithelial composite grade and stage scores in the proximal, mid-, and distal esophagus (Supplementary Table 5). Although lamina propria fibrosis was not a common finding among our cohort, if present, it improved significantly in the proximal esophagus, and had a nonsignificant trend toward improvement in the midesophagus and distal esophagus (Supplementary Table 5).

Endoscopic and Symptomatic Response

Exudates improved after treatment in 58% of patients ($P = .001$), furrows in 31% ($P = .02$), and edema in 31% ($P = .01$) (Table 3). The number of endoscopic abnormalities was reduced from a median of 3 (IQR, 2–3) to a median of 2 (IQR, 1–3) ($P < .01$) (Table 3). Inflammatory findings were reduced from a median of 2 (IQR, 2–3) to a median of 1 (IQR, 0–2) ($P < .001$) (Table 3). Rings were more frequent at the post-treatment endoscopy (8 vs 16; $P = .04$). There was a 25% reduction in the median number of symptoms: 4 (IQR, 3–6) vs 3 (IQR, 1–5) ($P = .003$) (Table 3). Several symptoms improved: chest pain (before: 10 [26%] vs after: 3 [8%]; $P = .04$), dysphagia (before: 17 [44%] vs after: 6 [16%]; $P < .005$), and pocketing/spitting out food (before: 10 [28%] vs after: 3 [8%]; $P = .04$).

Resolution of all endoscopic abnormalities occurred in 7 of 21 (33%) histologic responders while this occurred in only 3 of 30 (15%) nonresponders (Table 4). Resolution of at least 1 symptom occurred in 25 (61%) patients after a 1FED, while 12 (29%) patients had resolution of all symptoms (Table 4). We did not observe a significant difference in resolution of at least 1 symptom between histologic responders (15 of 21; 71%) and nonresponders (10 of 20; 50%; $P = .21$).

Quality-of-Life Changes With Elimination of Cow's Milk

Paired data points before and after treatment were collected for 14 children (self-report) and 15 caregivers (Supplementary Table 6). Although not significant, we found a trend toward improved QOL and a moderate-large effect size for self-reported Generic Core Scales: overall (78 vs 82; $P = .38$; effect size, 0.48), psychosocial (72 vs 78; $P = .40$; effect size, 0.42), and social (80 vs 98; $P = .1$; effect size, 0.88), which met the threshold for a minimal clinically important difference. There was a trend for lower parent-reported scores after a 1FED with a moderate-to-large effect size for domains: social (95 vs 80; $P = .18$; effect size, 0.53), psychosocial (90 vs 78; $P = .29$; effect size, 0.37), and emotional (90 vs 70; $P = .31$; effect size, 0.38), which met the threshold for a minimal clinically important difference. Thus, we found a dissociation of overall QOL between children and their parents/caregivers. For the self-reported PedsQL EoE module, there was a trend toward higher scores with a moderate-to-large effect size for the Symptoms II (66 vs 78; $P = .17$; effect size, 0.47) and Worry (69 vs 77; $P = .06$; effect size, 0.76) subscales. There were no significant differences before and after the 1FED for the EoE-QOL module completed by parents/caregivers.

Predictors of Treatment Response

Lastly, we explored potential predictors of treatment response. No differences were seen in sex, race, or ethnicity. Histologic responders had a nonsignificant trend toward being older: 12 years (IQR: 6–15 y) vs 7 years (IQR: 5–10 y) ($P = .06$) (Supplementary Table 7). No differences were noted in atopic comorbidities, although a nonsignificant trend toward decreased IgE-mediated food allergy was seen with histologic responders (19% vs 45%; $P = .10$). Among the family histories, there was a nonsignificant increase in celiac disease for histologic nonresponders (5% vs 25%; $P = .09$). Regarding medication use at the time of enrollment, histologic nonresponders more commonly carried an EpiPen (14% vs 60%; $P = .004$) and took inhaled corticosteroids (0% vs 25%; $P < .05$). Skin prick testing and food-specific IgE testing did not have predictive capacity for the response to a 1FED (Supplementary Table 7). A binary logistic regression model identified age and carrying an EpiPen as independent predictors of treatment response (Supplementary Table 8). Thus, the 1FED was more successful in older patients without anaphylactic food allergy.

Discussion

Dietary therapy for EoE is recommended as first-line treatment for EoE,[25] but highly restrictive diets can be difficult to adhere to long term.[11,26] Current standard-of-care elimination dietary treatment protocols in EoE exclude 4 to 8 foods from the diet.[7,12,27] However, excluding multiple foods from the diet, even temporarily, is challenging to maintain because it imposes a significant burden for adequate nutrient and micronutrient

intake. Therefore, identifying less-restrictive diets is of interest. In this study, we showed that exclusion of all CMP induces histologic remission in more than 50% of children with EoE. This was a large single-center prospective study assessing the efficacy of a 1FED (milk) for the treatment of EoE.

Prior work has identified variable histologic remission rates of 44% to 65% to milk elimination.[14,17–21] Kruszewski et al[17] found improvement in 65% of children (13 of 20), however, in their cohort, PPI-refractory EoE was not established with an endoscopy and their patients were treated concurrently with both PPI and milk elimination. In a retrospective cohort, Wong et al[18] reported 58 of 102 children who had histologic remission after 8 to 12 weeks of a 1FED, consistent with our findings. A recent prospective randomized study assessed the efficacy of 1FED vs 4FED and found similar improvements in validated symptom, histology, and quality-of-life scores. This study was restricted to children ages 6 and up, and did not extend the treatment duration for cross-contamination.[19] Our study validates CMP as a critical food trigger of eosinophilic inflammation, and removal of CMP alone reduces eosinophilia in more than half of children with EoE. We observed endoscopic improvement in 59%, with complete resolution of all endoscopic abnormalities in 24%. This is similar to Wong et al,[18] who reported resolution of inflammatory endoscopic abnormalities in 24% of patients treated with 1FED. However, there was a surprising increase in the frequency of rings after a 1FED. Rings, an early sign of fibrostenosis, were found in 20% of patients at baseline, and mild rings may have been under-recognized in the presence of inflammatory changes. Finally, we observed symptomatic improvement in 61% of patients and resolution of all symptoms in 29% of patients. Kliewer et al[19] reported significantly improved symptom scores with a 1FED, although there was greater improvement with a 4FED. Interestingly, we saw greater symptom improvement as well in our prospective 4FED study.[28] Thus, this study validates that the 1FED (milk) is sufficient to achieve all aspects of remission, clinical, endoscopic, and histologic, in a meaningful group of children with EoE.

Elimination diets are difficult, particularly when elimination of multiple types of food is needed. Diet elimination therapy increases the risk of malnutrition and nutritional deficiencies because patients often face a significant loss of calories and micronutrients, such as calcium and vitamin D.[27] Although a number of patients dropped out of the study before the second endoscopy, only 3 patients were unable to tolerate the diet. A key reason for this was the nutritional guidance by a dietitian to ensure calorie and micronutrient needs and assess for cross-contamination and this was also a key strength of our study. Notably, a subset of patients reported improved QOL for social and worry domains, suggesting the psychosocial effects of a 1FED may be limited, as compared with broader elimination.[11] Further studies are needed to understand long-term QOL in children treated with a 1FED.

We previously identified female sex and asthma as predictors of a successful response to a 4FED, while family history of food allergy and food sensitization by IgE were predictors of poor response.[12] In this study we found younger patients and patients with IgE-mediated food allergy were more likely to fail a 1FED. Finally, we found allergy testing had a poor correlation with identified EoE food triggers, similar to prior results from our group and others.[9,12,29]

The major strengths of this study were the prospective design and the number of subjects recruited, which improve generalizability. In addition, we used the validated EoE-HSS to show structural improvements in basal zone hyperplasia and dilated intercellular spaces in addition to eosinophilia. The EoE-HSS was evaluated at 3 levels of the esophagus (proximal, mid-, and distal), and identified a variable response, with the proximal esophagus most responsive to treatment, and the distal esophagus the least responsive to treatment. Incorporation of validated QOL measures identified novel perspectives of the 1FED between patients and their parents/caregivers. We identified discordant QOL scores for various overall and EoE-specific domains. Although small sample size may play a role, this finding raises interesting questions that future studies can address.

Our study had limitations as well. The study design intended to enroll 54 patients over 5 years, yet only 41 underwent endoscopy. This may have limited the significant differences we identified; however, this was a large single-center report of children with EoE following a 1FED prospectively. We did not randomize patients to placebo or another treatment arm. A placebo effect has been seen in medication trials,[30] but there are no placebo (or sham-diet) controlled studies of dietary elimination in EoE. The lack of a validated symptom questionnaire may have limited our ability to detect symptom improvement, although dysphagia, a core EoE symptom, improved in a significant number of patients. We saw a reduction in the number of symptoms in our subjects. In addition, our study may have experienced selection bias because recruitment of this study overlapped with our 4FED study.[12] Both studies identified CMP as the predominant trigger of EoE. Finally, our study did not determine the impact of PPIs with a 1FED because most patients continued PPI during the study. A recent abstract identified improved histologic response to a PPI with the addition of a 4FED.[31] However, it remains unknown if stopping a PPI before starting a 1FED would have altered the treatment response. Studies that randomize to diet vs diet/PPI could address the possible additive impact of PPI to response.

In summary, we prospectively identified histologic remission in 1 of 2 children with EoE with a significantly less-restrictive diet than SFED or 4FED. Significant improvement in symptoms, and endoscopic and histologic abnormalities, were achieved with the 1FED in a majority of patients. Notably, a 1FED does not require food re-introduction, thus transition to maintenance occurs more quickly without additional endoscopy. This has significant implications on the standard of care, and further studies could assess the optimal “step-up” approach, which has been shown previously to be feasible in adults.[13] Our results provide evidence that CMP elimination can be offered as an alternative to other elimination diets as first-line treatment for EoE.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations used in this paper:

1FED	1-food elimination diet
4FED	4-food elimination diet
CMP	cow's milk protein
EoE	eosinophilic esophagitis
eos/hpf	eosinophil per high-power field
HSS	histologic scoring system
IQR	interquartile range
PEC	peak eosinophil count
PPI	proton pump inhibitor
QOL	quality of life
SFED	6-food elimination diet

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What You Need to Know

Background

Eosinophilic esophagitis (EoE) is a chronic allergic–inflammatory disorder of the esophagus mostly triggered by food antigen(s); elimination diets excluding 2, 4, and 6 foods are effective but difficult to implement and maintain. Cow's milk protein is the most common identified trigger of inflammation.

Findings

Exclusive elimination of cow's milk protein induces histologic remission and improves endoscopic abnormalities and symptoms in more than 50% of children with EoE.

Implications for patient care

This single-milk-protein elimination diet represents an easy-to-accomplish, first-line approach to dietary elimination therapy for EoE.

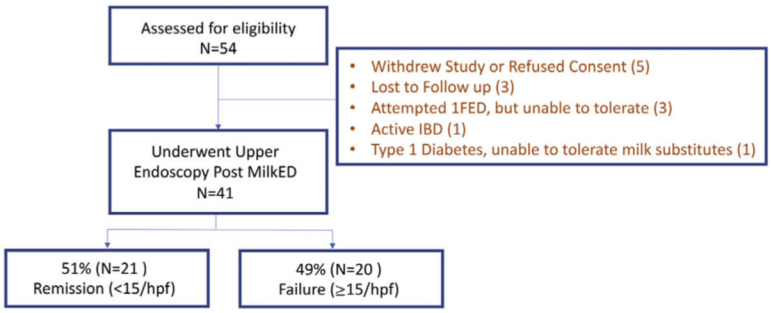

Figure 1.

Consort diagram showing study population. 1FED, 1-food elimination diet; hpf, high-power field; IBD, inflammatory bowel disease; MilkED, milk elimination diet.

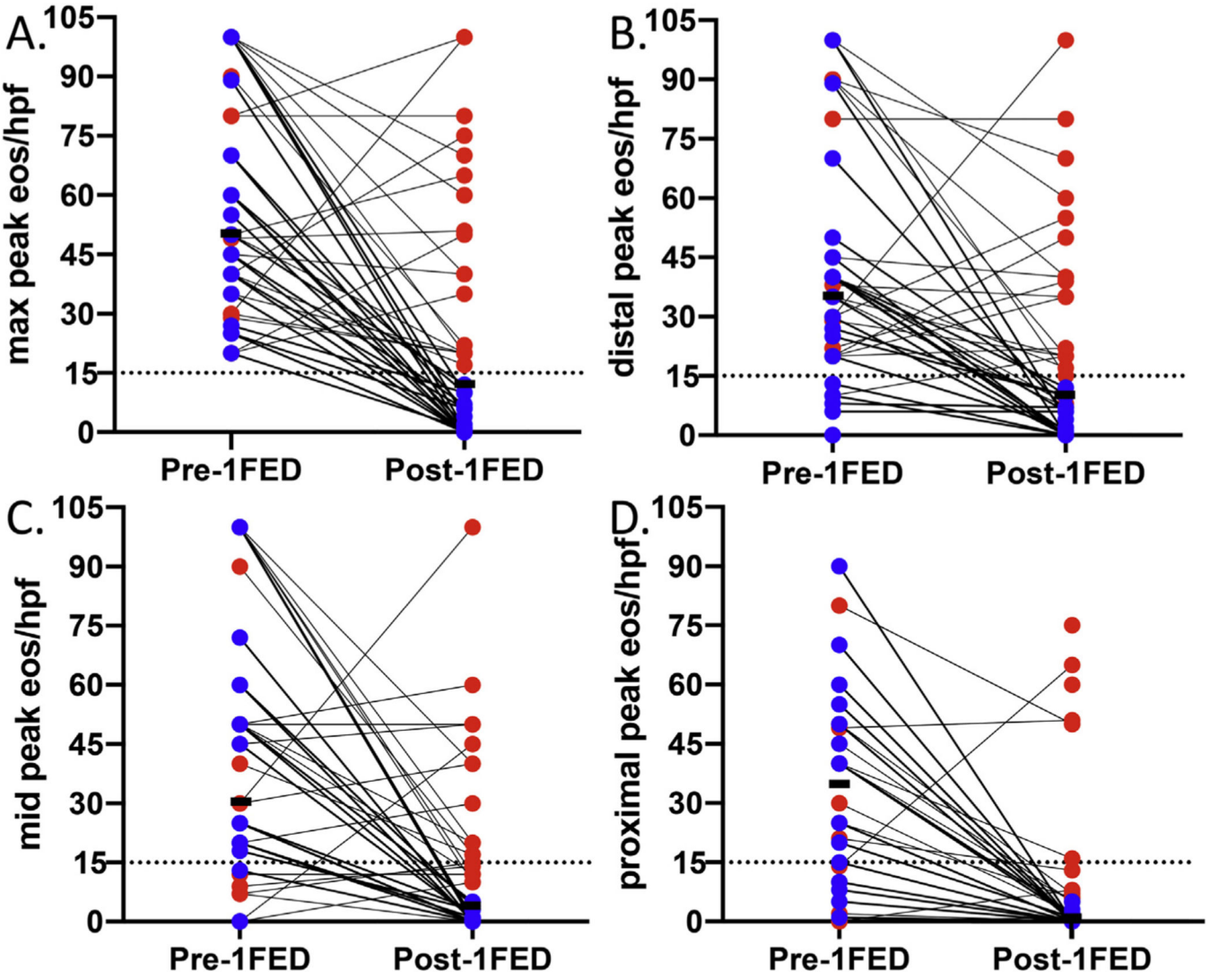

Figure 2.

(*A*) Peak eosinophil counts before and after 1FED. Reduced eosinophilia with milk elimination in the (*B*) distal, (*C*) mid-, and (*D*) proximal esophagus. The median is shown in black. Histologic responders are shown in blue, and nonresponders are shown in red. 1FED, 1-food elimination diet; eos/hpf, eosinophils per high-power field. Dotted line at histologic threshold for active EoE (15 eos/hpf).

Table 1.

Baseline Demographic, Clinical, Endoscopic, and Histologic Characteristics

	Overall (N = 41)
Demographics, n (%)	
Age, *y*, mean [IQR]	9 [6–13]
Male	31 (76)
White	36 (88)
Hispanic	2 (5)
Atopy/comorbidities, n (%)	
Allergic rhinitis	27 (66)
Asthma	14 (34)
Conjunctivitis	2 (5)
Drug allergy	6 (15)
Eczema	10 (24)
Gastroesophageal reflux disease	6 (15)
IgE-mediated food allergy	13 (32)
Family history, n (%)	
Allergic rhinitis	26 (63)
Asthma	22 (54)
Celiac disease	6 (15)
Colitis	2 (5)
Crohn’s disease	2 (5)
Eczema	13 (32)
EoE	6 (15)
Esophageal stricture	5 (12)
IgE-mediated food allergy	15 (37)
Gastroesophageal reflux disease	21 (51)
Hiatal hernia	7 (17)
Medications at enrollment, n (%)	
Proton pump inhibitor	37 (90)
Antihistamine	11 (27)
Bronchodilator	8 (20)
EpiPen (carries)	15 (37)
Inhaled corticosteroid	5 (12)
Intranasal corticosteroid	7 (17)
Montelukast	4 (10)
Topical steroid	0 (0)
Skin prick test, n (%)	
Any abnormal (n = 23)	15 (65)
Milk abnormal (n = 18)	2 (11)
Food sensitization on RAST, n (%)	
Any abnormal (n = 23)	18 (78)

	Overall (N = 41)
Milk abnormal (n = 21)	9 (43)
Prior treatment, n (%)	
Swallowed steroid[a]	8 (20)

EoE, eosinophilic esophagitis; IQR, interquartile range; RAST, radioallergosorbent test.

[a]Swallowed steroids included fluticasone inhaler or viscous budesonide.

Table 2.

Change in PEC and EoE-HSS Score After 1FED in Pediatric EoE

	n	Pretreatment	n	Post-treatment	*P* value[a]
Histology, median [IQR]					
Overall	41	50 [35–80]	41	12 [1–40]	**<.001**
Distal esophagus	41	35 [20–45]	41	10 [1–35]	**<.001**
Midesophagus	41	30 [18–60]	41	4 [0–17]	**<.001**
Proximal esophagus	30	35 [11–50]	40	1 [0–7]	**<.001**
EoE HSS score					
Grade					
Distal esophagus	39	9 [8–12]	39	5 [2–6]	**<.001**
Midesophagus	38	9 [6–13]	38	4 [1–5]	**<.001**
Proximal esophagus	27	7 [3–11]	27	2 [1–5]	**<.001**
Stage					
Distal esophagus	39	9 [6–10]	39	3 [1–5]	**<.001**
Midesophagus	38	9 [5–11]	38	2 [0–5]	**<.001**
Proximal esophagus	27	6 [4–10]	27	1 [0–4]	**<.001**

NOTE. Significant values are bolded $P < .05$.

EoE-HSS, eosinophilic esophagitis histologic scoring system; IQR, interquartile range; 1FED, 1-food elimination diet; PEC, peak eosinophil count.

[a]Comparison by Wilcoxon signed-rank test.

Table 3.

Change in Endoscopic Abnormalities and Symptoms With 1FED in Pediatric EoE

	n	Pretreatment	n	Post-treatment	*P* value[a]
Endoscopic findings, n (%)					
Edema	41	32 (78)	41	22 (54)	**.01**
Exudate	41	24 (59)	41	10 (24)	**.001**
Furrows	41	32 (78)	41	22 (54)	**.02**
Rings	41	8 (20)	41	16 (39)	**.04**
Stricture	41	0 (0)	41	1 (2)	ND[b]
Inflammatory sum,[c] median [IQR]	41	2 [2–3]	41	1 [0–2]	**<.001**
Sum,[b] median [IQR]	41	3 [2–3]	41	2 [1–3]	**.009**
Symptoms, n (%)					
Abdominal pain	41	13 (32)	38	16 (42)	.45
Chest pain	39	10 (26)	37	3 (8)	**.039**
Dysphagia	39	17 (44)	38	6 (16)	**.002**
Early satiety	35	15 (43)	37	16 (43)	1.00
Feeding difficulties	39	10 (26)	37	9 (24)	1.00
Food impaction	38	10 (26)	38	5 (13)	.15
Gagging/choking	37	7 (19)	37	2 (5)	.22
Heartburn	37	9 (24)	37	8 (22)	1.00
Nausea	38	10 (26)	38	10 (26)	.77
Odynophagia	37	5 (14)	37	1 (3)	.22
Pockets or spits out food	36	10 (28)	37	3 (8)	**.039**
Poor appetite	37	10 (27)	37	5 (14)	.13
Reflux or regurgitation	36	11 (31)	36	8 (22)	.69
Slow eating	38	19 (50)	37	11 (30)	.11
Vomiting	41	14 (34)	38	7 (18)	.15
Night wakening	35	7 (19)	35	3 (9)	.51
Symptom sum,[d] median [IQR]	41	4 [3–6]	38	3 [1–5]	**.003**

NOTE. The Wilcoxon signed-ranked test was used for paired endoscopy and symptom scores. Significant values are bolded, $P < .05$.

IQR, interquartile range; 1FED, 1-food elimination diet; ND, not determined.

[a]Comparison by McNemar test was performed for dichotomous paired data.

[b]Sum of edema, exudate, rings, furrows.

[c]Sum of edema, exudate, and furrows.

[d]Sum of symptoms that are present.

Table 4.

Outcomes of 1FED on Histologic, Endoscopic, and Clinical Metrics in Pediatric EoE

	Overall	Responder[a]	Nonresponder[a]
EGD to assess histologic response to CM elimination, n	41	21	20
Resolution of ≥1 endoscopy finding(s), n (%)[b]	24 (59)	13 (62)	11 (55)
Resolution of all endoscopic findings, n (%)[b]	10 (24)	7 (33)	3 (15)
Resolution of ≥1 symptoms, n (%)[b]	25 (61)	15 (71)	10 (50)
Resolution of all symptoms, n (%)[b]	12 (29)	4 (19)	8 (40)

CM, cow's milk; EGD, esophagogastroduodenoscopy; EoE, eosinophilic esophagitis; 1FED, 1-food elimination diet.

[a]A responder was defined by a peak eosinophil count fewer than 15 eosinophils per high-power field on esophageal biopsy specimens after a 1FED.

[b]The percent denominator is the column total.