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Role of Food and Aeroallergen Sensitization In Adult Eosinophilic Esophagitis

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Keywords

eosinophilic esophagitis; food allergy

Introduction

Eosinophilic esophagitis (EoE) is an emerging chronic inflammatory disease that affects both children and adults [1]. The disease is characterized by signs and symptoms of esophageal dysmotility from underlying chronic inflammation of the esophagus. Histologically, EoE is characterized by eosinophilic infiltration into the esophagus that persists after a proton pump inhibitor (PPI) trial. Chronic inflammation leads to histologic remodeling of the esophagus inclusive of fibrosis, rings, linear furrows, and stricture formation [2]. Symptoms vary between children and adults; while children tend to present with vomiting, abdominal pain and/or failure to thrive, adults often complain of dysphagia, food impaction and heartburn.

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The hypothesis that foods are triggers for EoE has been supported by the success of various food elimination diets. Since the first description of a successful food elimination diet in 1995 [3], many additional studies have validated these findings. EoE resolution rates in children treated with an amino acid based diet are 96% or higher [4–6]. An elemental diet also improves endoscopic and histological features of EoE in 72% of adults [7]. Empiric 4 or 6 food elimination diets also lead to resolution of EoE in more than 70% of adult subjects [8–10], and sequential reintroduction of foods are able to uncover specific trigger foods of EoE. Although efficacious, empiric elimination diets are also often cumbersome, time consuming, costly, unpalatable (particularly an elemental diet) and may induce iatrogenic nutritional deficiencies. Thus, more targeted approaches to food elimination have been sought.

Although IgE mediated skin testing does not appear to be an accurate predictor of EoE food triggers in adults [2, 5, 11–13], we sought to determine whether the identification of food and/or aeroallergen sensitivity in EoE patients may provide other significant clinical information about the patient and/or their disease. More specifically, does the presence of food or aeroallergen sensitivity identify a distinct phenotype of adult EoE? To address this question, we performed a retrospective chart review on adult patients with EoE within our University of Wisconsin Health System clinics. With these data, we examined whether food allergen sensitivity or aeroallergen sensitivity identify distinct clinical phenotypes of EoE.

Methods

We performed an IRB approved retrospective chart review of patients with a diagnosis of EoE (based on ICD-9 codes) seen at the University of Wisconsin Hospital and Clinics during the years 2008–2013. Of the total 724 patients, 257 were seen in a University of Wisconsin Hospital and Clinics Adult Allergy clinic. All 257 patient charts were accessed to capture demographics, atopic history, disease severity, endoscopy results, pathology reports, allergy test results, medical management and patient reported outcomes.

Patient demographic information included age at presentation, ethnicity, race and sex. History of atopic diseases was based on patient report and/or physician diagnosis as documented in the medical record. Disease severity was assessed by duration of EoE symptoms, history of emergency department visits for EoE symptoms and need for procedural interventions for EoE complications. Peripheral eosinophilia was defined as a peripheral eosinophil count of greater than 500. Endoscopy findings were obtained from a patient's initial diagnostic upper endoscopy procedure note. Eosinophils per high-powered field were recorded based on patient endoscopic esophageal pathology report. If multiple eosinophil counts were recorded, the highest number was used. If the report stated a count of "greater than x", it was recorded as such. A patient's medical management for EoE was based on documentation from the initial visit in the Allergy clinic and included medications for EoE, food avoidance strategies and procedural interventions. The pre-allergy management was based on the Allergist's documentation of management prior to the initial Allergy clinic visit. Post-Allergy visit medical management was based on the Allergist's documentation of recommendations at the initial encounter visit. Patient outcomes were determined by patient symptom report at a subsequent follow up visit with either

Gastroenterology or Allergy. Outcomes were categorized based on subjective evaluation of the clinic visit note as “complete improvement”, “partial improvement”, “no change” or “worse”. There were a number of patients that did not return to either Gastroenterology or Allergy clinics after their initial evaluation and were listed as “lost to follow up”. If any specific information was not available for a patient, then “unknown” was recorded for that entry.

Skin prick test (SPT) results were obtained from the patient’s medical record. A positive SPT result was recorded if there was any skin reaction to testing, which included trace reactions. For those patients with indeterminate SPT due to a blunted histamine reaction or positive saline reaction, “indeterminate” was recorded. In these cases, serum specific IgE results for foods and/or aeroallergens were recorded instead, if available. If no SPT was completed, but serum specific IgE to foods and/or aeroallergens were done, then results of the serum specific IgE were recorded. Any serum specific IgE greater than 0.35 kU/ml was considered positive. Patients were categorized as either “food sensitive” or “non-food sensitive” based on food SPT and/or serum IgE results.

For statistical analyses, the chi-squared test for association was used to compare categorical characteristics or outcomes by food sensitization status and aeroallergen sensitization status. Unknowns were included in the analysis. Because eosinophil counts per high powered field were often recorded as “greater than x” and were thus right censored, they were compared between groups using a parametric lognormal survival regression model. A p-value less than 0.05 was regarded as statistically significant.

Results

Of the total 257 patients seen at a University of Wisconsin Hospital and Clinics Adult Allergy Clinic, 155 patients (60%) were male and 102 patients (40%) were female. The average patient age was 38 years old (range 13 – 83 years). Four patients (2%) self identified as Hispanic/Latino ethnicity. The remainder of the patients that reported an ethnicity identified themselves as non-Hispanic. Most patients (97%) identified their race as white, followed by black (1%) and Hawaiian/Pacific Islander (1 patient). A majority (84%) of patients had concurrent atopic diseases such as asthma (43%), allergic rhinitis (79%), food allergy (21%) and atopic dermatitis (9%). In regards to reported food allergy, peanut/tree nut allergy was most common (35%), followed by fish/shellfish allergy (32%).

As shown in Table 1, the most commonly reported symptoms of EoE included dysphagia (81%), food impaction (58%) and symptoms of gastroesophageal reflux disease (GERD) (47%). In subjects’ whose medical record documented duration of EoE symptoms, almost 90% had EoE symptoms for over 1 year. Emergency Department (ED) visits for EoE symptoms, emergency procedures for food impaction and dilations were seen in 28%, 18% and 39% of patients respectively. A majority of patients’ whose chart documented a peripheral eosinophil count did not have peripheral eosinophilia (76%). Common esophageal endoscopy findings included esophageal rings (56%), linear furrows (35%), and strictures (40%). The most common recommended treatment for EoE was swallowed steroid (74%) followed by proton pump inhibitor (70%). Food avoidance was recommended in 40%

of cases, though we did not capture whether the food elimination was based on targeted recommendations from the food allergy testing or empiric elimination. Additionally, food avoidance was often recommended in addition to other medical therapies. Food avoidance as the sole treatment recommendation was only recommended in 10 patients. 32 patients were recommended to try food avoidance in addition to a PPI. In the patients with known outcomes, regardless of recommended treatment, there were no significant differences in the reports of complete improvement, partial improvement, or no change in symptoms (Figure E1).

IgE-mediated testing to foods, by SPT and/or serum specific IgE, was completed for 238 (92%) of the 257 adult EoE patients. Food SPT was performed for 224 (87%) patients with nine patients having uninterpretable results due to either blunted histamine response or dermatographism. Of these nine patients, seven had food specific serum IgE testing completed in addition to the SPT and the remaining two patients had no additional testing done. Excluding these two patients without interpretable results, there were a total of 236 patients with results in the form of SPT and/or serum specific IgE. A total of 56 (22%) patients had food specific serum IgE results: 42 patients had food specific IgE done in combination with food SPT and 14 patients had food specific IgE done only.

Of the 236 patients with interpretable IgE-mediated testing, 128 (54%) had a positive result to at least one food. As shown in Figure 1, of the six foods most commonly tested, peanut sensitivity was the most prevalent (51%), followed by soy (35%). Cod was the least common food sensitivity (8%). A complete list of food sensitivities is provided in the online supplement (Table E1).

A summary of aeroallergen sensitivity results is shown in Figure 2. SPT to aeroallergens was completed for 181 (70%) of the 257 adult EoE patients of which 5 had non-interpretable results. Of the five patients with non-interpretable SPT results, two had aeroallergen serum specific IgE completed and three patients did not have any additional testing done. An additional 2 patients had serum aeroallergen specific IgE done without any SPT. Of the 180 patients with interpretable aeroallergen test results, 157 (87%) were sensitized to at least one aeroallergen. Tree, dust mite and pet (cat and/or dog) sensitivities were the most common, affecting 70%, 69% and 66% of the patients, respectively.

In order to determine whether patient allergic sensitivities impact the clinical or biological characteristics of EoE, patients were stratified as food sensitive versus non-food sensitive based on food IgE-mediated testing (SPT and/or serum specific IgE) and stratified as aeroallergen sensitive versus non-aeroallergen sensitive based on aeroallergen IgE-mediated testing. As shown in Table 2, 128 patients were sensitized to at least one food and 108 patients had no food sensitivities. Patient characteristics did not differ between groups, except food sensitive patients were more likely to report concomitant asthma ($p=0.01$), allergic rhinitis ($p=0.02$), food allergy ($p<0.001$), or atopic dermatitis ($p=0.03$) compared to non-food sensitive patients. Patient reported EoE symptoms and duration of symptoms did not significantly differ between groups. Number of patients requiring ED visits for EoE signs or symptoms, emergency endoscopy for food impaction and esophageal dilations did not significantly differ between groups. Additional analyses were done to compare patients

with one or more food sensitivities with a history of a true IgE mediated food allergy and patients with food sensitivities without a history of a correlating IgE mediated food allergy (online supplement Table E2). There were no statistically significant differences in patient clinical characteristics between these two groups.

When patients were stratified by aeroallergen sensitivity, 157 patients were sensitized to at least one aeroallergen and 23 patients had no aeroallergen sensitivities (Table 2). Patient characteristics did not differ between groups, except aeroallergen sensitive patients were more likely to report concomitant asthma ($p=0.017$) and allergic rhinitis ($p<0.001$) compared to non-aeroallergen sensitive patients.

The distribution of peripheral eosinophil counts was comparable regardless of food or aeroallergen sensitivity (Table 3). The endoscopy findings of esophageal rings and linear furrows were commonly observed in all patient groups, 51–61% and 28–35%, respectively. Strictures were noted more often in aeroallergen sensitive ($p=0.021$) patients. In contrast, esophageal felinezation was observed more often in non-aeroallergen sensitive patients ($p=0.003$).

As shown in Table 4, Allergist treatment recommendations consisted primarily of proton pump inhibitor and/or swallowed steroid. As expected, food avoidance was recommended significantly more often for food sensitive patients compared to non-food sensitive patients (77% vs 9% respectively, $p<0.001$). The majority of patients reported symptomatic improvement at a subsequent follow up visit, and this did not significantly differ between the groups of food sensitive and non-food sensitive patients. Additionally, the recommendation of food avoidance for those patients who were food sensitive did not lead to differences in patient reported outcomes (Figure E1).

Esophageal biopsy eosinophils per high-powered-field (hpf) were analyzed with a parametric lognormal survival regression model. Eosinophil counts did not differ between food sensitive and non-food sensitive individuals (Figure 3A), or between aeroallergen sensitive and non-aeroallergen sensitive individuals (Figure 3B). It should be noted that were a few patients in each group that had biopsy eosinophils per hpf less than 15. These patients were still considered to have EoE per their gastroenterologist, due to other classical endoscopy findings consistent with the disease (rings, linear furrows).

Discussion

Our findings are consistent with previously published reports that suggest that identification of IgE-mediated food sensitivities do not necessarily predict EoE trigger foods [11, 12]. We sought to further address whether there was another benefit to performing IgE based testing in adult EoE patients, specifically identifying a different clinical phenotype of adult EoE. To this end, we examined clinical and pathophysiological features of EoE to determine whether patients with food or aeroallergen sensitivity exhibited differences compared to patients without sensitivity.

There are several limitations to our study. A notable limitation to this study is the retrospective design without a standardized evaluation of EoE patients. There are now

validated instruments for endoscopic and symptom scoring that would be essential for future prospective evaluations of EoE [14, 15]. Due to the retrospective nature of this study, we were unable to determine if patients were treated with a PPI prior to their endoscopic diagnosis. We recognize that this is a significant limitation, as this is now part of the diagnostic criteria for EoE. Likewise, our chart review was unable to establish why some patients did not have IgE mediated food and/or aeroallergen testing done. This is likely due to the fact that there is no standardized allergy evaluation in adult EoE, and the decision to perform allergy testing is based on provider discretion. An additional limitation is that our study only reflects the characteristics of patients with EoE seen in an allergy clinic. It is our experience that the decision to refer a patient with EoE to an Allergist is provider specific. However, it should be noted that our results reflect a subgroup of adult EoE patients and therefore might not apply to all adult EoE patients. It is possible that a more distinct phenotype of the disease would have been apparent had all the EoE patients been studied.

Our data show that identification of IgE-mediated food sensitivity does reveal a patient population that is in general more atopic, but otherwise does not distinguish a distinct clinical phenotypic of adult EoE. There were no significant clinical differences in patient demographics, patient reported symptoms, duration of symptoms, severity of disease, endoscopic findings, esophageal pathology, treatment or patient reported outcomes when comparing food sensitive versus non-food sensitive patients. We acknowledge that patient outcomes were subjective and did not include validated tools to assess follow up endoscopy, histologic examination, or patient related outcome measures [14–16].

Similarly, the identification of IgE-mediated aeroallergen sensitivity showed no significant clinical differences in patient demographics, patient reported symptoms, duration of symptoms, severity of disease, esophageal pathology, treatment or patient reported outcomes. A significant finding was that the endoscopy in aeroallergen sensitive patients more often revealed strictures. It is intriguing to consider whether this suggests differences in fibrotic versus inflammatory processes in the esophageal tissue. It is also notable that felinization was found less often in patients with aeroallergen sensitization, but this finding was relatively rare overall.

The role of targeted elimination diets based on allergy skin testing is unclear. Earlier studies showed success rates in children of 53% and 65% by using allergen patch testing and skin testing, respectively, to identify culprit foods [4, 17]. Recent studies demonstrated sensitization to food allergens in 50–82% of adult EoE patients [18, 19]. The most commonly identified food allergens were peanut, soy, egg, milk and tree nuts [20] as well as wheat, tomato, carrots and onions [19]. While adults with EoE commonly have a high rate of food sensitization, this sensitization rarely connotes actual food allergy or correctly identifies a causative agent for EoE [5]. In a study by Straumann et al., 29% of adult patients had sensitization to milk, egg, fish or seafood, but this was clinically relevant in only one patient [2]. Molina-Infante et al. treated 15 adult EoE patients with a targeted elimination diet and only 5 out of 15 had complete or partial histologic resolution of their EoE [11]. Gonsalves et al. found that retrospectively, skin prick testing would have only predicted 13% of trigger foods in adult EoE patients undergoing empiric elimination diets [12]. A recent systematic review of the various elimination diets reinforced the growing evidence that

allergy-testing directed elimination diets are among the least successful elimination diets in adults, with an overall effectiveness of 32% [13]. Our study also failed to identify any clinical phenotypic difference associated with IgE-mediated food sensitivity.

EoE is considered an atopic disease and is commonly associated with other allergic diseases such as allergic rhinitis, asthma and atopic dermatitis [21, 22]. The pathogenesis of EoE is similar to that of other atopic conditions, primarily involving Th2 inflammation resulting in esophageal tissue expression of mediators such as eotaxin-3, IL-13, and IL-5 [23–25]. Experimentally, EoE can also be induced in a mouse model by intrinsic Th2 cytokines such as IL-13 and IL-5 [26, 27]. Studies have demonstrated seasonal peaks of EoE symptoms and diagnosis, correlating with pollen seasons, suggesting a potential role of aeroallergens in the pathogenesis of EoE [28–30]. Prior studies have demonstrated aeroallergen sensitization in 86–93% of adult EoE patients [18, 19]. Experimentally, EoE has been induced by intranasal exposure to aeroallergens in mice [31]. Additionally, experimental epicutaneous allergen sensitization may potentially prime the body for respiratory allergen-induced EoE [32]. In a study with 63% of adult EoE patients exhibiting IgE mediated food sensitization, a majority of the patients were sensitized to foods that cross react with the pollens [21]. Most notably, these adult patients were sensitized to wheat and rye, which is cross-reactive with grass pollen. However, an elimination diet of wheat and rye failed to improve EoE symptoms in sensitized patients [33].

Our data confirm that there is no utility in identifying food IgE-mediated sensitivity for EoE in adult patients. The most notable finding from this study regarding potential phenotypes of EoE was the differing prevalence of strictures and fibrosis noted on endoscopy in aeroallergen versus non-aeroallergen sensitive subjects. This observation coupled with the findings of aeroallergen involvement in EoE in humans and mouse models suggest that evaluation for aeroallergen sensitivity could be important as a phenotypic distinction in EoE. Future prospective studies are needed to determine whether aeroallergen sensitivity truly defines a distinct phenotype of EoE, whether there are differences in the pathophysiology of EoE, and whether there is clinical relevance to the identification of aeroallergen sensitive EoE.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

ED	Emergency Department
EoE	Eosinophilic Esophagitis

EOS	Eosinophil
ICD-9	International Classification of Diseases-9 th revision
IRB	Institutional Review Board
SPT	Skin Prick Testing
GERD	Gastroesophageal Reflux Disease
Hp	High Powered Field
PPI	Proton Pump Inhibitor

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Figure 1. Food Sensitivities. The percentage of patients that exhibited a positive skin prick test or serum IgE test for the specified food allergens is shown.

Figure 2.
Aeroallergen Sensitivities. The percentage of patients that exhibited a positive skin prick test or serum IgE test for the specified aeroallergens is shown.

Figure 3.

Eosinophil levels on esophageal biopsy. The eosinophil (EOS) count per high power field (HPF) is represented as a cumulative proportion of patients (on y-axis) that have less EOS count per HPF listed (on x-axis). **A)** The food allergen sensitive (Blue) and non-food allergen sensitive (Red) patients were compared. **B)** The aeroallergen sensitive (Orange) and non-aeroallergen sensitive (Green) patients were compared.

Table 1

EoE Clinical Characteristics

Clinical Characteristics	Number of Patients (%) N=257
Symptoms	
Dysphagia	209 (81%)
Food Impaction	148 (58%)
GERD	212 (82%)
Nausea/Vomiting	22 (9%)
Abdominal Pain	12 (5%)
Regurgitation	16 (6%)
Chest Pain	17 (7%)
Choking	18 (7%)
Other	19 (7%)
Duration of Symptoms	
<1 year	29 (11%)
1–5 years	72 (28%)
5–10 years	30 (12%)
>10 years	75 (29%)
Unknown	50 (49%)
Severity	
ED Visit	71 (28%)
Procedure-FI	46 (18%)
Dilation	100 (39%)
Peripheral Eosinophils	
>500	43 (17%)
<500	137 (53%)
Unknown	77 (30%)
Endoscopic Findings	
Rings	143 (56%)
Furrows	89 (35%)
Strictures	102 (40%)
Treatment Recommendation	
PPI	179 (70%)
H2 Blocker	27 (10%)
Swallowed Steroid	189 (74%)
Oral Prednisone/Entocort	12 (5%)
Montelukast	11 (4%)
None	4 (2%)
Food Avoidance Total (with or without other treatments)	103 (40%)
Food Avoidance Only	10 (4%)

Clinical Characteristics	Number of Patients (%) N=257
Food Avoidance + PPI Only	32 (12%)
PPI and Swallowed Steroid	133 (52%)
Any Combination of >1 Medicine	150 (58%)
Reported Outcomes	
Partial Improvement	39 (15%)
Complete Improvement	118 (46%)
Worse	4 (2%)
No Change	23 (9%)
Unknown	73 (28%)

Table 2

Comparison of Clinical Characteristics Stratified by Allergen Sensitivity

	Food Sensitive Patients		Aeroallergen Sensitive Patients	
Patient Characteristics	Yes (n=128)	No (n=108)	Yes (n=157)	No (n=23)
Symptoms				
Dysphagia	101 (79%)	90 (83%)	128 (82%)	21 (91%)
Food Impaction	69 (54%)	68 (63%)	86 (55%)	17 (74%)
GERD	66 (52%)	43 (40%)	79 (50%)	10 (43%)
Nausea/Vomiting	12 (9%)	9 (8%)	12 (8%)	2 (9%)
Abdominal Pain	6 (5%)	4 (4%)	10 (6%)	1 (4%)
Regurgitation	11 (9%)	5 (5%)	10 (6%)	2 (9%)
Chest Pain	10 (8%)	8 (7%)	10 (6%)	2 (9%)
Choking	10 (8%)	3 (3%)	10 (6%)	0 (0%)
Other	20 (16%)	10 (9%)	22 (14%)	4 (17%)
Duration of Symptoms				
<1 Year	13 (10%)	13 (12%)	13 (8%)	4 (17%)
1–5 Years	29 (23%)	37 (34%)	42 (27%)	6 (26%)
5–10 Years	15 (12%)	14 (13%)	21 (13%)	3 (13%)
>10 Years	43 (34%)	27 (25%)	50 (32%)	4 (17%)
Unknown	27 (21%)	17 (16%)	30 (19%)	6 (26%)
<10 Years	57 (44%)	64 (59%)	76 (48%)	13 (57%)
>10 Years	43 (34%)	27 (25%)	50 (32%)	4 (17%)
Unknown	27 (21%)	17 (16%)	30 (19%)	6 (26%)
Patient Reported History of Atopic Disease				
Allergic Rhinitis	107 (84%) *	76 (70%)	155 (99%) **	11 (48%)
Asthma	66 (52%) *	37 (34%)	80 (51%) *	5 (22%)
Food Allergy	41 (32%) **	12 (11%)	41 (26%)	4 (17%)
Atopic Dermatitis	16 (12%) *	4 (4%)	17 (11%)	0 (0%)
Disease Severity				
Dilation (at any time)	57 (44%)	39 (36%)	64 (41%)	5 (22%)
ED	32 (25%)	37 (34%)	35 (22%)	19 (39%)
Procedure for Food Impaction Removal	24 (19%)	20 (18%)	26 (17%)	5 (22%)

*
p<0.05**
p<0.01

Table 3

Comparison of Patient Laboratory and Endoscopic Findings Stratified by Allergen Sensitivity

	Food Sensitive Patients		Aeroallergen Sensitive Patients	
Patient Characteristics	Yes (n=128)	No (n=108)	Yes (n=157)	No (n=23)
Peripheral Eosinophil Count				
Eos >500	19 (15%)	21 (19%)	29 (18%)	2 (9%)
Eos <500	78 (61%)	50 (46%)	84 (54%)	11 (48%)
Unknown	31 (24%)	37 (34%)	44 (28%)	10 (43%)
Endoscopic findings:				
Gastritis/Duodenitis	17 (13%)	8 (7%)	13 (8%)	4 (17%)
Esophageal Inflammation	14 (11%)	7 (6%)	10 (6%)	2 (9%)
Plaques	12 (9%)	6 (6%)	10 (6%)	3 (13%)
Erosions/Ulcers	10 (8%)	10 (9%)	8 (5%)	3 (13%)
Erythema	3 (2%)	2 (2%)	3 (2%)	0 (0%)
Hiatal hernia	16 (12%)	20 (18%)	26 (17%)	3 (13%)
Fibrosis/Thickening	5 (4%)	1 (1%)	6 (4%)	1 (4%)
Rings	68 (53%)	66 (61%)	80 (51%)	12 (52%)
Linear Furrows	42 (33%)	38 (35%)	45 (29%)	8 (35%)
Felination	7 (6%)	5 (5%)	1 (1%)	3 (13%) ^{**}
Schatzki Ring	11 (9%)	8 (7%)	13 (8%)	0 (0%)
Stricture	59 (46%)	37 (34%)	71 (45%) [*]	4 (17%)
None of the Above	21 (16%)	15 (14%)	15 (10%)	2 (9%)
Unknown	15 (12%)	11 (10%)	22 (14%)	2 (9%)

*
p<0.05**
p<0.01

Table 4

Comparison of Patient Treatment Recommendations and Reported Outcomes Stratified by Allergen Sensitivity

	Food Sensitive Patients		Aeroallergen Sensitive Patients	
Patient Characteristics	Yes (n=128)	No (n=108)	Yes (n=157)	No (n=23)
Allergy Recommended Treatment				
Swallowed Steroid	87 (68%)	85 (79%)	118 (75%)	19 (82%)
PPI	93 (73%)	73 (68%)	107 (68%)	16 (69%)
H2 Blocker	12 (9%)	8 (7%)	17 (11%)	4 (17%)
Prednisone/Entocort	8 (6%)	4 (4%)	7 (4%)	1 (4%)
Montelukast	5 (4%)	5 (5%)	7 (4%)	0 (0%)
No Treatment	1 (1%)	3 (3%)	2 (1%)	0 (0%)
PPI and Swallowed Steroid	66 (52%)	57 (53%)	81 (52%)	14 (61%)
Combination of Medications	73 (57%)	63 (58%)	92 (59%)	15 (69%)
Food Avoidance	98 (77%) ^{**}	10 (9%)	76 (48%)	6 (65%)
Patient Reported Outcomes				
No Change	10 (8%)	11 (10%)	16 (10%)	1 (4%)
Partial Improvement	18 (14%)	11 (10%)	27 (17%)	3 (13%)
Complete Improvement	66 (52%)	46 (43%)	75 (48%)	10 (43%)
Worse	1 (1%)	2 (2%)	2 (1%)	1 (4%)
Unknown	33 (26%)	37 (34%)	37 (24%)	8 (35%)

^{**}
p<0.01