Main Project:
Evaluation of Growth Outcomes in Children with Eosinophilic Esophagitis

Background

Eosinophilic esophagitis (EoE) is a chronic inflammatory disease characterized by eosinophilic infiltration of esophageal epithelium. Children with EoE typically present with vomiting, feeding dysfunction, and failure to thrive. Diagnosis of EoE is based on these clinical symptoms and histological evidence of eosinophilic infiltration upon biopsy of esophageal epithelium. Treatments for EoE currently include topical steroids (fluticasone, budesonide), dietary therapies, and endoscopic dilation.

EoE is thought to be an allergic disease with the underlying pathogenesis related to exposure to food allergens. Accordingly, dietary therapies are effective first line treatments for EoE. Strategies for dietary treatment include selective elimination diets, in which potential food allergens are removed from the diet, and elemental formulas, in which hypoallergenic liquid formulations are administered as the sole source of nutrition. Response rates for these approaches are comparable to those achieved by pharmacological therapy.

Growth and development is a major concern for pediatric EoE patients, as feeding dysfunction and restrictive diets can prevent patients with EoE from receiving sufficient nutrient intake. Moreover, elimination diets can lead to poor growth if nutritional replacements for the eliminated food are not provided. Milk and wheat, both highly important parts of a child’s diet, are the two most common allergic triggers of EoE. Use of elemental formulas can circumvent these disadvantages because they provide a complete source of nutrients, and therefore may be able to help children with EoE achieve normal growth. However, outcomes related to growth and EoE-specific treatments have never been examined, and this is a major gap in knowledge.

To date, elemental diets, elimination diets, and other EoE treatments have only been compared for their effectiveness in producing clinical and histological remissions. Growth has not been extensively assessed as a specific outcome, and the various treatment modalities have not been compared with respect to growth outcomes. Analyzing these differences could help pediatric gastroenterologists and nutritionists guide the treatment of pediatric EoE patients and select optimal treatment and nutritional approaches.

Aims
We aim to assess growth outcomes by treatment types in children with EoE.

Hypothesis
We predict that EoE patients who take elemental formula will have better growth outcomes.

Methods
Our study population included all children (<18) diagnosed with EoE at University of North Carolina Hospitals (Chapel Hill, NC). We reviewed records from 2005-2014. To assess growth, we included patients who had at least 3 visits, sufficient height/weight information for these three visits, and were being actively treated for their EoE with steroids, or dietary therapy.

This study was a retrospective cohort study. Data on age, demographics, clinical symptoms, endoscopic features, histological findings, anthropometric measures (height, weight, growth velocity), treatment approaches and adherence, and frequency of encounters with the physician was extracted using a standardized case report form.

Results
We identified 123 participants who met our inclusion criteria for the study. Of these, 99 (80.49%) were male and 24 (19.51%) were female. On average, patients had 9.6 follow up visits, and 33.42 months between their first and last visit. The average age of participants on their first visit was approximately 87 months, and the average BMI and BMI percentiles were 17.28 and 50.05% respectively. The most common treatment choice was topical (swallowed) steroids, with 347 (56%) visits having steroids as the prescribed treatment modality. An additional 168 (27%) visits involved treatment using a combination of both steroids and a form of dietary therapy (Figure 1). On average, visits in which patients were prescribed a combination dietary therapy (both elimination and elemental diets) reported the highest BMI percentile, and visits in which patients were prescribed elemental formulas reported the lowest BMI percentiles (Figure 2). Similarly, when graphing the change in BMI percentile as a function of time since the initiation of treatment, complete and supplemental formulas have the most negative slopes (-0.8109 and -1.7479 respectively; Figure 3). However, elimination diets were found to have the most positive slope (0.925), followed by steroids alone (0.4387) (Figure 3).

Figure 1. Pie chart illustrating percentage of visits by prescribed treatment modality at the time of that visit.

Figure 2. Average BMI Percentile of EoE patients by treatment.

Figure 3. Change in BMI Percentile vs. months since treatment initiation for patients undergoing single modality treatment.

Discussion
Topical steroids, elimination diets, and elemental formulas are all effective first-line therapies for EoE, but previous studies have not assessed how these treatments affect the growth outcomes. The aim of this study is to assess growth outcomes by treatment type in children who have EoE. Our results show that patients who received elemental formulas as treatment were found to have the worst growth outcomes (Figures 2,3), whereas patients who received steroids and elimination diets had much better growth outcomes. This is in contrast to our hypothesis.

One possible explanation for this finding is that patients often receive elemental formula either as a sole source of nutrition or as nutritional supplementation, as a response to poor feeding and/or failure to thrive, thus potentially biasing this patient group to lower BMI percentiles. The results may therefore represent selection bias – sicker children at baseline receive elemental formula, and because they are more ill they are less likely to grow well. Moreover, patients seemed to have a greater ability to adhere to a steroid regimen than elimination or elemental diets. While these points have not been supported by data in this preliminary analysis, data on failure to thrive symptoms and adherence were collected in the study and will be quantified in the final analyses. Also, because the percentage of patients who received elemental formulas was considerably lower than those receiving steroids and elimination diets, these differences may not be statistically significant. However, continuation of this study will include more data from other sites in the Carolina Eosinophilic Esophagitis Collaborative (CEoEC), and we expect that these sites will increase our sample of patients who were treated with elemental formula, and provide more power for the analyses.

For this study, to which I devoted the majority of my time during the CMSRP, my participation was as follows. I assisted in writing the IRB application, which was approved prior to beginning this project. I developed the on-line data extraction tool. I personally reviewed the medical records of over 200 pediatric subjects and extracted the pertinent data using the on-line tool. Finally, I performed the preliminary analysis as noted above, and will continue to be involved in additional data extraction and analysis going forward. The plan is to have preliminary data submitted as an abstract to a national GI (DDW) meeting this winter.

Additional Projects:

Grocery Study

Although diet therapies, such as the six-food elimination diet and elemental formula, are effective first-line therapies for EoE, the cost of these therapies can be prohibitive to patients. In addition to studying the growth outcomes of children on these therapies, I also evaluated the real-world costs and shopping burden of adhering to one of these diets: the six-food elimination diet (SFED). In this study, a dietician with expertise in EoE created calorie- and nutrient-matched diets for an unrestricted diet and an SFED. We then priced these diets at standard and specialty grocery stores in 12 different US cities. We found that the SFED costs more than the unrestricted diet when shopping at a standard grocery store (~$650/year), and many items included in the SFED are only found in the specialty grocery store, thus increasing the shopping burden of patients by requiring them to make an extra trip. These added costs and burdens can be communicated to patients when they decide between pharmacological therapy and dietary therapy for EoE.

The final paper detailing these findings has been submitted for publication, and I am the second author.

Administration of propofol in patients with egg allergy: a systematic review

The last project I have started this summer is a systematic review on the use of propofol as a sedative for patients with egg allergies. This is very relevant to EoE because many EoE patients have food allergies, and diagnosis and management of EoE requires endoscopies, during which patients are administered propofol for sedation. I will be continuing to work on this project in the coming months.

References