## ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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#### Dietary Therapies and Eosinophilic Esophagitis



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#### **G&H** What are the treatment goals for eosinophilic esophagitis?

NG Treatment for eosinophilic esophagitis (EoE) focuses on targeting different endpoints, including histologic, endoscopic, and symptomatic remission. Although it is not clear which of these is the most important, improvement in all is necessary to properly treat this disease. When striving for histologic remission, gastroenterologists try to reduce eosinophil levels as much as possible, but a good target is under 15 eosinophils per high-power field. The goals of endoscopic remission include the improvement of inflammatory features of EoE and the addressing of any underlying strictures. Good treatment goals are to improve these inflammatory endpoints and to strive for an esophageal stricture diameter of greater than 16 to 17 mm. The most common symptom of EoE in adults involves difficulty swallowing or feeling food pass more slowly or become caught in the esophagus. Thus, a treatment goal is to ensure that patients are eating unencumbered without having to limit their diet or modify the consistencies of their food. Once all 3 of these endpoints of remission are met, optimal treatment has typically been achieved.

#### **G&H** What treatment strategies are currently available to manage EoE?

NG EoE treatment consists of the 3 Ds: drugs, diet, and dilation. First-line therapy for EoE can be either medical or dietary therapy. Because there are currently no medications approved by the US Food and Drug Administration to treat EoE, current medical options are limited to swallowed topical corticosteroids. The most common formulations that have been used are swallowed fluticasone (which is dispersed in either an aerosolized inhaler or a powdered discus form), oral viscous budesonide, or a budesonide slurry. Treatment doses for swallowed topical fluticasone range from 2 to 4 puffs of the inhaler twice daily based on the severity of disease. For patients with significant inflammation and/or stricturing, the full dose twice daily is recommended, whereas patients with moderate disease are better suited to 2 puffs twice daily. When using the oral viscous budesonide solution, a 1-mg dose taken twice daily is beneficial. With the budesonide solution, patients are instructed to mix the solution with either sucralose or honey to make it a viscous consistency. Patients using either medication should undergo endoscopy after 8 to 12 weeks to ensure that the therapy is working. Once endpoints of histologic, endoscopic, and symptomatic remission are met, the dosing can be reduced to once daily, as maintenance therapy is needed in this disease.

The second most common approach to treating EoE is dietary therapy. The 3 diets that have been tried most

often are the elemental diet, allergy testing-directed diet, and empiric elimination diet. The elemental diet, which was first evaluated in pediatric patients in the 1990s, is a formula-based, allergen-free diet in which patients drink an amino acid-based formula as their sole source of nutrition. This approach is likely the most effective of the dietary therapies, with prior meta-analyses showing an effectiveness of approximately 91%. However, there are significant limitations to using elemental formula,

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including palatability, cost, and the long reintroduction period that is necessary to identify food triggers. For these reasons, an elemental diet is not typically used in adult patients with EoE. Another strategy is an allergy testingdirected diet, which involves eliminating foods based on the results of available allergy testing such as skin prick or atopy patch testing. However, current available allergy tests check for immunoglobulin E (IgE)-mediated diet reactions or anaphylactic-type reactions, and EoE is not an IgE-mediated condition, making this approach the least-effective dietary strategy, with improvement in only 40%. Due to these limitations, the empiric elimination diet, which involves removing common food allergens (milk, wheat, soy, egg, nuts, and seafood) that are triggers in EoE, is a favored approach to dietary therapy. The elimination of these 6 foods is known as the 6-food elimination diet and is approximately 70% to 74% effective in children and adults, respectively; therefore, it is the longest-studied and most-effective empiric elimination diet used.

The third treatment approach to EoE is focusing on esophageal dilation and improving esophageal stricturing and the overall caliber of the esophagus, which can contribute to dysphagia and food impaction. Dilation is typically reserved until after an initial course of either medical or dietary therapy, as both treatments can improve esophageal caliber. If strictures are persistent despite treatment, conservative esophageal dilation can be performed safely in patients with EoE.

# **G&H** What are the advantages and disadvantages of the various diet-based therapies?

NG EoE is considered a chronic immune-mediated reaction of the esophagus typically triggered by dietary food antigens. The major advantage of diet-based therapies is that patients can potentially identify the root cause of their disease and, by doing so, can avoid the foods that are their triggers instead of relying on a daily medication. Because both dietary and medical therapies are very effective treatments, patients are often the main drivers in deciding which is the right treatment plan for them. For most patients, the main motivation to pursue dietary therapy is to avoid a daily medication. The most common dietary treatment plan revolves around the empiric elimination diet. It is important to note that the main goal of empiric elimination diet is not to be on a restricted diet indefinitely, but to reintroduce eliminated foods to identify the likely culprit. However, this can be a long process depending on how restrictive a diet plan is and should be discussed with the patient ahead of time. Follow-up endoscopy during dietary intervention is needed to assess for disease inflammation, and this should also be reviewed prior to starting this treatment plan.

## **G&H** What challenges are associated with modifying patients' dietary lifestyles?

**NG** Any type of diet can be challenging. The difficulty lies in being strict about the diet plan; when clinicians are advocating that patients eliminate certain foods in an EoE diet, they are advocating that patients eliminate all ingredients in every single food, similar to what is being advised for food anaphylaxis. This requires a lot of reading of labels and necessitates many changes in the types of food that patients would otherwise buy. It also limits their ability to eat out freely because of cross-contamination with foods that can inadvertently occur with eating at a restaurant and not in the patient's own kitchen. Patients are counseled on being able to communicate all of their allergens and diet restrictions to the waitstaff or chefs and are provided with resources on how to do so effectively. However, certain external factors can be difficult to control. For instance, being away at college, traveling extensively for work, and relying solely on restaurant outings

can create challenges for adherence to diet elimination. In these circumstances, patients may be counseled to hold off on dietary therapy until life becomes a little simpler.

Interestingly enough, due to coronavirus disease 2019, many patients are now not eating out or traveling, and they are actually gravitating toward a diet plan because they have much more control over their eating styles than they did previously. Typically, I avoid having patients start dietary therapy before the holidays because the most restrictive part of the diet is during the first 6 weeks, but without the usual winter holiday celebrations and parties, more patients are interested in starting this dietary therapy.

### **G&H** What factors should be considered when choosing a specific dietary approach to follow?

NG The choice of diet and of treatment for EoE in general is very individualized and depends on what best fits the lifestyle of the patient. My colleagues and I use a shared decision approach in our practice and discuss available options with our patients and which option may fit best for them. There are many empiric elimination diet approaches with different rates of effectiveness. The 6-food elimination diet, which eliminates milk, wheat, soy, egg, nuts, and seafood, is approximately 70% to 74% effective over 6 weeks. The 4-food elimination diet, which eliminates milk, wheat, soy, and egg, is approximately 45% to 60% effective over 6 weeks. If patients were to eliminate just the top 2 allergens-milk and wheat-that approach is approximately 30% to 40% effective over 6 weeks. In children, a milk-only elimination diet has been 65% effective, and this approach is currently being studied in adults. There is also a step-up elimination diet, which starts by eliminating 1 or 2 foods and subsequently eliminating more if the less-restrictive approach is not working. I cannot stress enough that there is no best approach; therefore, discussing these options with patients and making an individualized plan is most effective. Some patients may want to eliminate several foods and, if that approach is not successful, move onto medical therapy. Other patients may decide to follow the 6-food elimination diet because it is the most effective upfront. For patients who do not have fish in their diet or who cannot eat nuts, the 4-food elimination diet may be a better fit; foods that patients have no interest in eating typically should not be reintroduced into their diet. It is important for the clinician and patient to discuss needs and interests when choosing a therapy and participate in a shared decision-making approach.

## **G&H** What is the long-term adherence of dietary therapies?

NG Several studies have looked at patients who have continued dietary therapy, and the adherence at 1 year or longer is approximately 50%. Of the 50% who remain on the diet, studies have shown that 100% maintained remission. However, 50% of patients discontinued the diet for various reasons, whether it was too restrictive, too difficult with traveling or work, or other factors interfered. My colleagues and I performed a survey study in which we followed patients on the 6-food elimination diet over time, and we found that almost 60% of patients stayed on the diet. Patients who did not remain on the diet reported concerns of overall psychological burden, such as being too restricted on a diet plan and how it limited certain social engagements for them. Interestingly, almost all of the patients in the study, regardless of whether they maintained long-term diet restriction, advised dietary therapy to other newly diagnosed EoE patients as a valuable way to identify food triggers.

It is important to emphasize to patients that eliminating a food trigger means removing it from their diet going forward. However, there might be times that they want to take in the food trigger (eg, a special event or holiday) or they cannot avoid it (eg, vacation). Then, a combined approach with medication may help, with the idea that the rest of the year they are going to be adhering to their diet. Use of medical therapy around those specific times can help improve quality of life in patients on restricted diets.

#### **G&H** Is dietary therapy considered a first-line treatment for patients with EoE?

**NG** Both medication and dietary therapy are considered first-line treatment for EoE. Both approaches are effective and tolerable; it is just a matter of patient preference and having clinical resources that can support these approaches. For instance, effective dietary therapy usually requires the expertise of a skilled nutritionist who can be helpful in providing nutritional counseling and monitoring adherence and contamination. At our multidisciplinary EoE clinic, my colleagues and I are fortunate to have a dedicated EoE dietitian to assist patients in these approaches.

#### **G&H** What are the priorities of research in this area?

**NG** One of the main priorities in EoE research as it pertains to a dietary approach is to find minimally invasive or noninvasive ways to follow treatment intervention and assess for esophageal inflammation so that patients who are going through dietary plans do not need to have follow-up endoscopy after every intervention. Some tests have been developed, such as the Esophageal String Test (EnteroTrack), Cytosponge (Medtronic), and unsedated transnasal endoscopy, but more research and development are needed to make these devices more readily available for use in EoE. It would also be beneficial to have an allergy test that identified upfront which foods are the triggers for each individual patient without having to go through an empiric elimination approach. The last area is identifying factors that predict long-term adherence and compliance on a diet to allow dietary treatment to be more successful for long-term management of EoE.

#### Disclosures

Dr Gonsalves serves on the advisory board of Allakos, is a consultant for Sanofi/Regeneron and AstraZeneca, receives

royalties from UpToDate, and is a speaker and serves on the steering committee for eosinophilic gastrointestinal disorders (Medscape).

#### **Suggested Reading**

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