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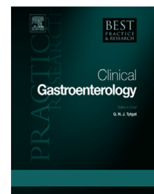

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Therapeutic strategies in eosinophilic esophagitis: Induction, maintenance and refractory disease

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A B S T R A C T

Eosinophilic esophagitis (EoE) is a chronic, immune-mediated disease that is increasingly recognized as one of the most common causes of dysphagia and foregut symptoms in adults and children. Topical corticosteroids, elimination diets, and esophageal dilations are effective options for both induction and maintenance therapy in EoE. Current pharmacologic options are being used off-label as no agent has yet been approved by regulatory authorities. Little is known about the natural history of EoE, however, raising controversy regarding the necessity of maintenance and therapy in asymptomatic or treatment-refractory patients. Furthermore, variability in treatment endpoints used in EoE clinical trials makes interpretation and comparability of EoE treatments challenging. Recent validation of a patient-related outcome (PRO) instruments, a histologic scoring tool, and an endoscopic grading system for EoE are significant advances toward establishing consistent treatment endpoints.

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Abbreviations: CRTH2, chemoattractant receptor-homologous molecule on Th2 cells; EOE, eosinophilic esophagitis; DSQ, dysphagia symptom questionnaire; EEsAI, eosinophilic esophagitis activity index; FLIP, functional luminal imaging probe; IL-5, interleukin-5; IL-13, interleukin-13; PRO, patient-related outcome; SFED, six-food elimination diet.

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Practice points

- Topical steroids and elimination diets are effective, first-line treatments for eosinophilic esophagitis.
- Natural history studies suggest that untreated eosinophilic esophagitis is a disease with progressive esophageal remodeling and fibrostenosis.
- Measures to assess therapeutic response in eosinophilic esophagitis include validated patient reported outcomes for symptoms and quality of life, histologic scores for eosinophilic inflammation, a validated grading system for endoscopic features, and biomarker panels depicting genetic expression in the esophageal mucosa.
- Esophageal dilation is an effective means of managing strictures that are not amenable to medical or diet therapies for eosinophilic esophagitis.
- Systemically delivered biologic therapies that target cytokines involved in the pathogenesis of eosinophilic esophagitis are being investigated as potential, disease modifying agents.

Research agenda

- Further studies are needed to more fully understand the natural history of eosinophilic esophagitis to better inform therapeutic decisions.
- Prospective studies evaluating both long-term maintenance treatment and combination therapy for eosinophilic esophagitis are awaited.
- Standardization of therapeutic endpoints in future studies will allow for better cross-comparability among clinical trials in eosinophilic esophagitis.
- Randomized, controlled trials of diet therapies will provide data to optimize the most appropriate use of this non-pharmacologic approach to the management of eosinophilic esophagitis.

Introduction

Over the past two decades, eosinophilic esophagitis (EoE) has emerged as one of the most common causes of dysphagia in children and adults. Studies have identified a number of medical, dietary and endoscopic therapies that are highly effective at remedying the symptoms, signs and histopathology of EoE. This review will focus on overall management strategies in EoE, specifically discussing the definition of therapeutic response, selection of initial therapy, controversies regarding the rationale for maintenance therapy and considerations for refractory disease.

Definition of response to therapy

The overall goals of therapy of EoE include alleviation of presenting symptoms as well as prevention of disease progression, improvement in quality of life and reversal of existing complications. Understanding the natural history of EoE is of central importance to a discussion of therapeutic goals. If EoE were a self-limited condition, short-term therapy or clinical observation would be appropriate. On the other hand, a chronic or progressive course would favor early intervention and maintenance therapy. Unfortunately, little is known regarding the natural history of EoE, creating a challenge in patient management, particularly in those with minimal symptoms. In the longest follow-up study to date, Straumann et al. followed 30 adult patients for an average of seven years in the absence of medical or diet therapy [1]. During the study period, all patients maintained a stable nutritional state, but 97% of patients continued to experience dysphagia. Dysphagia increased in 23%, was stable in 37% and

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