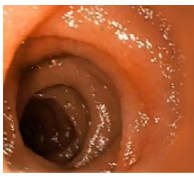


Targeting Pharmacotherapy to Effectively Manage Eosinophilic Esophagitis

Key Concepts

Introduction

Eosinophilic esophagitis (EoE) is a chronic allergic inflammation of the esophagus. It is initiated by a T-helper type 2 inflammatory reaction to specific food antigens, resulting in eosinophilic infiltration of esophageal tissues. Over time, this leads to chronic inflammation, fibrosis, and narrowing of the esophagus. Signs and symptoms include esophageal dysfunction, dysphagia, pain, and food impaction.[1] Infants and children are more likely to have feeding difficulties, nausea, vomiting, abdominal pain, and chest pain, whereas adolescents and adults more commonly present with heartburn, chest pain, food impaction, and solid food dysphagia.[2]

The etiology of EoE is thought to include immune dysfunction, environmental factors, and genetics.[1] Approximately 50% of patients with EoE have signs of allergy, and EoE frequently occurs alongside other type 2 inflammatory diseases, such as allergic rhinitis, asthma, atopic dermatitis, and food allergies.[2,3] EoE is often excluded from the differential diagnosis with these disorders, resulting in misdiagnosis and/or delay: up to 8 years in adults and up to 3.5 years in children.[4] Diagnostic delays, difficult treatment regimens, and the debilitating nature of EoE can lead to social and psychological distress.[1]

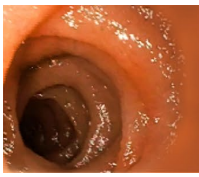
The prevalence of EoE is 34 and 42.2 cases per 100,000 among children and adults, respectively, and its incidence is rising.[5] EoE is seen worldwide, more commonly in cold and arid climates and in rural areas, and occurs more frequently in males, those younger than 50 years old, and in Caucasians.[6-8]

Screening and Diagnosis

A diagnosis of EoE requires the combination of symptoms of esophageal dysfunction, eosinophils in the esophageal mucosa, as well as the exclusion of other causes of esophageal eosinophilia. The esophagus is examined for signs including linear furrows, stacked circular rings, strictures, edema, white plaques, and pale fragile mucosa with congestion and loss of vascularity.[9] The presence of 15 or more eosinophils per high-power field is a diagnostic criterion.[10] Biopsy is required for diagnosis, with samples taken from at least 6 sites in the esophagus.[10]

Treatment Options

Standard-of-care therapy as recommended by the Joint Task Force for Allergy/Immunology Practice Parameters includes the off-label use of topical corticosteroids and proton pump inhibitors (PPI), as well as diet therapy (food elimination, elemental diets, nasogastric tube feeding) and esophageal dilation.[11] The histologic and symptomatic benefits of these medications are limited. Dupilumab is the only medication with an indication to treat EoE in adults and children aged 12 years and older, weighing at least 40 kg. Dysphagia improved significantly with dupilumab vs placebo in clinical trials, and nearly 60% of adults and children achieve histologic remission within 24 weeks.[12] Additional therapies are under investigation, including esophageal-targeted topical corticosteroid formulas, montelukast, disodium cromoglicate, purine analogues, and additional monoclonal antibodies.[13-15]



Targeting Pharmacotherapy to Effectively Manage Eosinophilic Esophagitis

Key Considerations

The incidence and prevalence of EoE are rising worldwide, due in part to improved disease recognition. The diagnosis of EoE requires endoscopic examination, histopathology, and the exclusion of other causes of esophageal eosinophilia. Comorbid Th2-mediated inflammatory diseases are common, including atopic and autoimmune conditions. Diagnostic delays are also common, and can increase the risk of long-term sequelae. Barriers such as cost and access to care have been associated with lack of follow-up, particularly once acute symptoms have resolved. Daily PPI therapy, which is low in cost, widely available, and easy to administer, has been the usual first-line treatment, followed by swallowed topical corticosteroids. Dupilumab has been approved in the United States for treatment of EoE in adults and children aged 12 years and older; guidelines that include its use are being updated. New therapies are at various stages of development. Shared decision making and comanagement among gastroenterologists, allergists, primary care and behavioral health providers, dietitians, and family members can improve adherence, care planning, treatment of common comorbidities, and enhance quality of life in individuals with EoE.

REFERENCES

1. Gómez-Aldana A, Jaramillo-Santos M, Delgado A, Jaramillo C, Lúquez-Mindiola A. Eosinophilic esophagitis: Current concepts in diagnosis and treatment. *World J Gastroenterol*. 2019;25(32):4598-4613. doi:10.3748/wjg.v25.i32.4598
2. Vinit C, Dieme A, Courbage S, et al. Eosinophilic esophagitis: Pathophysiology, diagnosis, and management. *Arch Pediatr*. 2019;26(3):182-190. doi:10.1016/j.arcped.2019.02.005
3. Reed CC, Dellon ES. Eosinophilic esophagitis. *Med Clin North Am*. 2019;103(1):29-42. doi:10.1016/j.mcna.2018.08.009
4. Shaheen NJ, Mukkada V, Eichinger CS, Schofield H, Todorova L, Falk GW. Natural history of eosinophilic esophagitis: a systematic review of epidemiology and disease course. *Dis Esophagus*. 2018;31(8). doi:10.1093/dote/doy015
5. Navarro P, Arias Á, Arias-González L, Laserna-Mendieta EJ, Ruiz-Ponce M, Lucendo AJ. Systematic review with meta-analysis: the growing incidence and prevalence of eosinophilic oesophagitis in children and adults in population-based studies. *Aliment Pharmacol Ther*. 2019;49(9):1116-1125. doi:10.1111/apt.15231
6. Jensen ET, Hoffman K, Shaheen NJ, Genta RM, Dellon ES. Esophageal eosinophilia is increased in rural areas with low population density: results from a national pathology database. *Am J Gastroenterol*. 2014;109(5):668-675. doi:10.1038/ajg.2014.47
7. Dellon ES, Jensen ET, Martin CF, Shaheen NJ, Kappelman MD. Prevalence of eosinophilic esophagitis in the United States. *Clin Gastroenterol Hepatol*. 2014;12(4):589-596.e581. doi:10.1016/j.cgh.2013.09.008
8. Dellon ES, Hirano I. Epidemiology and natural history of eosinophilic esophagitis. *Gastroenterology*. 2018;154(2):319-332.e313. doi:10.1053/j.gastro.2017.06.067
9. Dellon ES. Eosinophilic esophagitis: diagnostic tests and criteria. *Curr Opin Gastroenterol*. 2012;28(4):382-388. doi:10.1097/MOG.0b013e328352b5ef
10. Lucendo AJ, Molina-Infante J, Arias Á, et al. Guidelines on eosinophilic esophagitis: evidence-based statements and recommendations for diagnosis and management in children and adults. *United European Gastroenterol J*. 2017;5(3):335-358. doi:10.1177/2050640616689525
11. Hirano I, Chan ES, Rank MA, et al. AGA institute and the joint task force on allergy-immunology practice parameters clinical guidelines for the management of eosinophilic esophagitis. *Ann Allergy Asthma Immunol*. 2020;124(5):416-423. doi:10.1016/j.anai.2020.03.020
12. Dellon ES, Rothenberg ME, Collins MH, et al. Dupilumab in adults and adolescents with eosinophilic esophagitis. *N Engl J Med*. 2022;387(25):2317-2330. doi:10.1056/NEJMoa2205982
13. Lucendo AJ. Pharmacological treatments for eosinophilic esophagitis: current options and emerging therapies. *Expert Rev Clin Immunol*. 2020;16(1):63-77. doi:10.1080/1744666x.2019.1705784
14. Silva FMCE, de Oliveira EE, Ambrósio MGE, et al. Disodium cromoglycate treatment reduces T_H2 immune response and immunohistopathological features in a murine model of Eosinophilic Esophagitis. *Int Immunopharmacol*. 2020;83:106422. doi:10.1016/j.intimp.2020.106422
15. de Rooij WE, Dellon ES, Parker CE, et al. Pharmacotherapies for the treatment of eosinophilic esophagitis: State of the art review. *Drugs*. 2019;79(13):1419-1434. doi:10.1007/s40265-019-01173-2