ARTICLE

Diagnosis and management of eosinophilic oesophagitis

Varan Perananthan
Gastroenterologist[1]
Clinical Research Fellow[2]
PhD candidate[3]

Rebecca Burgell
Gastroenterologist[1]
Functional Gastrointestinal Disorders Service Head[1]
Adjunct Associate Professor (Research)[2]

[1] Department of Gastroenterology and Hepatology, The Alfred, Melbourne

[2] Monash University, Melbourne

[3] Clinical Pharmacology and Toxicology Research Group, Biomedical Informatics and Digital Health, The University of Sydney

Keywords
budesonide, dysphagia, endoscopy, eosinophilic oesophagitis, food bolus impaction, monoclonal antibodies, proton pump inhibitors

Aust Prescr 2024;47:20–5
https://doi.org/10.18773/austprescr.2024.005

SUMMARY

Eosinophilic oesophagitis is a chronic inflammatory disease related to food allergy that should be suspected in patients presenting with food bolus impaction, or a history of dysphagia with or without atopy. The 6 most common food triggers are animal milk proteins, wheat, eggs, soy, nuts and seafood.

Eosinophilic oesophagitis is a histological diagnosis with at least 15 eosinophils (60 eosinophils per mm^2) per high-power field on oesophageal biopsy. Alternative causes of oesophageal eosinophilia should be excluded.

Patients with eosinophilic oesophagitis require lifelong management. Depending on patient preference, this may involve dietary exclusion of confirmed food trigger(s) or pharmacological treatment. The mainstays of pharmacological treatment are swallowed topical corticosteroids and proton pump inhibitors, but several monoclonal antibodies are currently under investigation for treatment of eosinophilic oesophagitis.

Introduction

Eosinophilic oesophagitis is a chronic inflammatory condition of the oesophagus related to a non-immunoglobulin E (IgE)–mediated form of food allergy. Patients have increasing symptoms of dysphagia due to continued exposure to food antigens, but are often not diagnosed until they present with food bolus impaction.[1] Implicated antigens, known as triggers, vary between individuals and can include animal milk proteins, wheat, eggs, soy, nuts and seafood.[2,3] Patients often have only one food trigger, but some patients have multiple triggers. Most patients with eosinophilic oesophagitis have comorbid atopic conditions, such as asthma, allergic rhinitis and atopic dermatitis.[2]

In susceptible individuals, exposure to food antigens causes eosinophilic infiltration of the oesophagus and chronic inflammation, leading to deposition of subepithelial fibrous tissue. Over time, oesophageal remodelling and dysfunction occur.[4] Patients may develop trachealisation of the oesophagus and strictures, which cause dysphagia and food bolus impaction.[5] Symptoms are not a reliable guide to the severity of inflammation, and patients tend to experience dysphagia or food impaction after eating foods with a firm consistency (e.g. meat); however, these foods are not necessarily the triggers precipitating eosinophilia.

First described in 1993, the prevalence of eosinophilic oesophagitis has quadrupled in the last 30 years, from mean estimates of 15 per 100,000 people before 2007 to 63 per 100,000 people after 2017, becoming the second most common oesophageal disease after gastro-oesophageal reflux disease (GORD).[1,6] Eosinophilic oesophagitis is usually diagnosed in childhood or early adulthood, and has a 3:1 male predominance.[7] Although uncommon, eosinophilic oesophagitis can be first diagnosed in older adults.[8]

Eosinophilic oesophagitis is due to a combination of environmental and genetic factors; however, the cause of the rising prevalence is not completely understood. The condition is common among first-degree relatives and the frequency is 41% in monozygotic twins and 24% in dizygotic twins.[9]

Clinical assessment and indications for specialist referral

Clinical assessment is the first step when a diagnosis of eosinophilic oesophagitis is suspected. The most common symptoms of eosinophilic oesophagitis in adults are dysphagia and food bolus impaction;[10] other symptoms include chest pain and heartburn. Approximately 50% of patients presenting to the emergency department with food bolus impaction who require endoscopic intervention have eosinophilic oesophagitis.[11] Eosinophilic oesophagitis is also a common cause of spontaneous oesophageal perforation.[12]

In young children, symptoms of eosinophilic oesophagitis are nonspecific and can include failure to thrive, fussy eating, irritability, vomiting and abdominal pain.[13]

This article is peer-reviewed

The presence of other atopic conditions, such as asthma, allergic rhinitis and atopic dermatitis, or a family history of these conditions, increases the likelihood of a diagnosis of eosinophilic oesophagitis.

Any patient presenting with food bolus impaction, or a history of dysphagia with or without atopy, should be referred to a gastroenterologist for further evaluation. Other red flags that should trigger a referral include odynophagia (pain when swallowing), unexplained weight loss or persistent reflux despite treatment.

Early diagnosis and referral to a gastroenterologist is key to preventing the progression of fibrosis and development of strictures, reducing the rare risk of oesophageal perforation, and minimising impact on quality of life.

Differentiating between eosinophilic oesophagitis and GORD

Similarly to eosinophilic oesophagitis, GORD is associated with the presence of eosinophils in the oesophagus. GORD is the main differential diagnosis for eosinophilic oesophagitis, but distinguishing between the conditions can be difficult – key factors that can be helpful include symptoms, gender and history of atopic conditions.

Symptoms of GORD, such as heartburn, regurgitation, chest pain and acid taste in the mouth, also occur in eosinophilic oesophagitis, but dysphagia and food bolus impaction do not occur with GORD. Patients with eosinophilic oesophagitis are often symptomatic at the time of eating, whereas GORD symptoms usually occur after eating and at night.[14]

Response to proton pump inhibitors (PPIs) does not necessarily indicate GORD as the primary cause of oesophageal eosinophilia because patients with either GORD or eosinophilic oesophagitis may respond (or not) to PPIs.[15,16]

Eosinophilic oesophagitis has a 3:1 male predominance, compared with GORD, which has a 1:1 gender ratio.[7] A history of atopy also increases the likelihood of eosinophilic oesophagitis.

Diagnostic criteria

The diagnosis of eosinophilic oesophagitis can be made in an individual with typical clinical symptoms and biopsies of the oesophagus demonstrating at least 15 eosinophils (60 eosinophils per mm^2) per high-power field. It is also important to exclude alternative causes of oesophageal eosinophilia (see Box 1).[15]

The diagnostic work-up of eosinophilic oesophagitis is best performed by a gastroenterologist or immunologist, and interpretation of histological findings requires input from a pathologist.

Macroscopic features of eosinophilic oesophagitis can be visible on upper gastrointestinal endoscopic examination in some patients and are useful for assessing disease severity and complications.

Serum eosinophil concentration does not correlate with symptoms of eosinophilic oesophagitis, or response to treatment, and measurement is not useful in the diagnosis or management of eosinophilic oesophagitis. Skin tests and measurement of serum IgE concentration do not accurately identify implicated food antigens and should not be used.[17]

Oesophageal biopsy

An upper endoscopy duodenoscopy with biopsies is pivotal in the diagnosis of eosinophilic oesophagitis, and is required to access some treatments on the Pharmaceutical Benefits Scheme (PBS).

Biopsies should be obtained from at least 2 oesophageal sites, at least 5 cm apart, because distribution of eosinophilic oesophagitis can be

Box 1 Diagnostic criteria for eosinophilic oesophagitis based on expert consensus reached at the 2017 AGREE conference[15]

symptoms of oesophageal dysfunction, such as:

- dysphagia
- food bolus impaction
- food refusal
- heartburn
- regurgitation
- vomiting
- odynophagia
- chest pain

AND

histopathological confirmation with oesophageal biopsies exhibiting at least 15 eosinophils (60 eosinophils per mm^2) per high-power field

AND

exclusion of other causes of oesophageal eosinophilia, such as:

- gastro-oesophageal reflux disease
- eosinophilic gastrointestinal disease
- achalasia
- hypereosinophilic syndrome
- connective tissue disease
- Crohn disease
- infections
- pill-induced oesophagitis [NB1]
- graft versus host disease

NB1: Pill-induced oesophagitis refers to a direct toxic effect on the mucosa from an oral medication (e.g. a bisphosphonate or antibiotic).

patchy – ideally tri-level biopsies of the lower, middle and upper oesophagus should be obtained.[18] At the first upper endoscopy, biopsies should also be performed in the stomach and duodenum to exclude eosinophilic gastroenteritis as a differential diagnosis.[19]

Oesophageal biopsies are examined for the presence of raised eosinophils. The diagnostic threshold for eosinophilic oesophagitis is at least 15 eosinophils (60 eosinophils per mm^2) per high-power field.

GORD may have similar histological features to eosinophilic oesophagitis, including eosinophilia, but the eosinophil count is usually less than 5 eosinophils (16 eosinophils per mm^2) per high-power field.[14] Furthermore, in GORD the inflammation is usually restricted to the lower oesophagus whereas in eosinophilic oesophagitis the inflammation may be scattered throughout the oesophagus, hence the importance of tri-level biopsies.[14]

Macroscopic features on upper endoscopy

Macroscopic features of eosinophilic oesophagitis seen on upper endoscopy include oesophageal rings, furrows, white exudates and strictures; however, these are not always present.[5] Furrows, oedema and exudates frequently reappear with food challenges or cessation of effective treatment. Rings and strictures are slow to resolve and slow to reappear; strictures indicate chronic fibrosis.

The eosinophilic oesophagitis endoscopic reference score – referred to as the mnemonic 'EREFS' – is used to grade the severity of eosinophilic oesophagitis based on scoring individual endoscopic features. The total score provides an overall assessment of severity and can be used to guide management and assess treatment response (Table 1).[19]

Table 1 Eosinophilic oesophagitis endoscopic reference score[19]

Endoscopic feature	Description	Score
o**E**dema	decreased visibility of blood vessels	0 to 1
Rings	presence and severity of concentric rings (trachealisation) in the oesophagus	0 to 3
Exudates	amount of white plaque or patches adherent to the oesophageal mucosa	0 to 2
Furrows	presence and depth of linear furrows in the oesophageal lining	0 to 2
Strictures	presence and degree of narrowing or strictures in the oesophagus	0 to 1
		Total score out of 9

Treatment for adults

Overview of treatment

All patients with a diagnosis of eosinophilic oesophagitis require treatment and this is generally continued lifelong. Treatment is generally initiated by specialists, but primary care clinicians have an important role in the ongoing prescribing of drug treatment. This article focuses on treatment of adults only; treatment of children is outside the scope of this review.

Quality of life is often reduced in patients with eosinophilic oesophagitis. The goals of treatment are to reduce eosinophil count on oesophageal biopsy, improve quality of life, normalise swallowing function and prevent food bolus impaction events. Response can be achieved through dietary intervention or pharmacological treatment. The choice of approach is largely based on patient preference, rather than disease severity. Oesophageal biopsies are required to confirm response to treatment because symptoms alone are not reliable.

Dietary intervention involves identifying the specific food trigger(s) causing eosinophilic oesophagitis and avoiding consumption of that food in the future. However, the process of identifying food triggers requires multiple food elimination steps and oesophageal biopsies to assess response, and it can be difficult for patients to adhere to this process.

Pharmacological treatment options have evolved over the past few years; current treatment options include swallowed topical corticosteroids and PPIs. No specific pharmacological treatment is considered first line; however, orodispersible budesonide tablets may be preferred because of their demonstrated high efficacy.

Dietary intervention

Dietary intervention, often implemented with input from a dietitian, involves identifying the specific food trigger(s) causing eosinophilic oesophagitis and avoiding consumption of that food in the future.[2] The 6 most common triggers for eosinophilic oesophagitis are: animal milk proteins, wheat, eggs, soy, nuts and seafood.[3,20]

Two dietary approaches are commonly used in practice – the step-down and the step-up approaches.[21] The **step-down approach** (more appropriate for patients with severe disease) involves exclusion of all 6 common food triggers at once, with an upper endoscopy performed after 4 to 6 weeks. If remission is achieved, the triggers are reintroduced one by one, with repeat upper endoscopy after each food is reintroduced to check for relapse. The

advantage of this method is the high efficacy, with a meta-analysis showing histological remission in up to 68% of patients.[22] Disadvantages include the need for multiple upper endoscopies, poor adherence related to extreme dietary restriction, and higher risk of nutritional deficiencies.[22]

The **step-up approach** (best used in patients with mild to moderate symptoms) involves initially excluding 2 common triggers (animal milk proteins and wheat). If remission is demonstrated on upper endoscopy after 4 to 6 weeks, either animal milk proteins or wheat is trialled alone to identify the specific trigger. If remission is not achieved, further food exclusion steps are undertaken to identify the trigger.[20] The advantage of this approach (compared with the step-down approach) is that food triggers may be identified earlier, thus avoiding unnecessary dietary restrictions. The disadvantage is that it is less effective than the step-down approach, with smaller studies showing histological remission in 40 to 55% of patients.[22]

Swallowed topical corticosteroids

Swallowed topical corticosteroids are the mainstay of treatment for eosinophilic oesophagitis and are generally continued lifelong in the absence of dietary intervention.

In the past a 'budesonide slurry' was used; the formulation is prepared by mixing budesonide nebulising solution (used 'off label') with a carrier to create a viscous mixture. While this formulation had a reasonable efficacy – randomised controlled trials showed symptom improvement and histological response in 64% of patients – its use was limited by the requirement for patients to prepare the slurry.[23]

Use of the budesonide slurry has now been replaced by an orally disintegrating tablet formulation.[24] The formulation is mucoadhesive, which allows budesonide to adhere to the oesophageal mucosa providing prolonged local release of drug and reduced systemic absorption, which minimises adverse effects.[25]

In clinical trials, the reported clinical and histological remission rate for orodispersible budesonide was 85% after 12 weeks;[24] however, longer-term data have shown a clinical and histological remission rate of 75%.[26] Further studies have found symptoms of oesophageal dysfunction persist in 15% of patients even with histological remission,[27] which may be due to ineffective delivery of medication, residual mild oesophageal strictures, narrow oesophageal calibre or decreased oesophageal distensibility. Regardless, a meta-analysis has shown that this formulation of budesonide is the most effective therapy currently available for eosinophilic oesophagitis in adults.[28]

To qualify for induction therapy with orodispersible budesonide on the PBS, patients must have a clinical history consistent with eosinophilic oesophagitis and histological confirmation of at least 15 eosinophils (60 eosinophils per mm^2) per high-power field, and must be treated by a gastroenterologist, or a surgeon or physician experienced in the management of eosinophilic oesophagitis. Maintenance therapy can be prescribed, in consultation with one of the above-mentioned specialists, if a follow-up upper endoscopy after 8 weeks of induction treatment shows histological remission (defined as less than 5 eosinophils [16 eosinophils per mm^2] per high power field).

The following advice should be provided to patients to maximise efficacy of orodispersible budesonide:

- adhere to treatment
- take the tablet after eating a meal
- allow the tablet to dissolve on the tip of the tongue before swallowing
- ensure the process of dissolving the tablet takes 2 to 5 minutes
- after administration, wait 30 minutes before eating, drinking, performing oral hygiene activities (e.g. toothbrushing, flossing) or using other oral medications, to avoid diluting the medication.

Candidiasis in the mouth, pharynx or oesophagus is the most frequently observed adverse effect. In clinical trials, the frequency was not dose related and the cases were of mild to moderate severity.[24,26] Patients can be treated with topical or systemic antifungal therapy, as appropriate, while continuing treatment with orodispersible budesonide.

Proton pump inhibitors

Proton pump inhibitors (PPIs) are an appropriate treatment option and widely used in eosinophilic oesophagitis.

Although eosinophilic oesophagitis is not an acid reflux disorder, concurrent acid reflux, which is common, can exacerbate oesophageal inflammation and symptoms. By reducing the acidity of the stomach contents that refluxes into the oesophagus, PPIs may alleviate oesophageal irritation. Reducing acidity may also improve the integrity of the oesophageal mucosal barrier to food triggers.

PPIs are also known to modulate immune responses and inhibit pro-inflammatory cytokines, such as interleukin (IL)-6, IL8 and tumour necrosis alpha. These anti-inflammatory effects may mitigate the eosinophilic inflammation.[29] Furthermore, PPIs may

exert pH-independent effects by influencing certain factors that are critical for the inflammatory cascade, such as chemokines, adhesion molecules and growth factors.[30] This may influence the recruitment or activation of eosinophils.

The response to PPIs in eosinophilic oesophagitis is typically modest – PPIs are estimated to elicit a histological response in 40 to 50% of patients.[22,31] If response to treatment is confirmed on oesophageal biopsy, PPIs should be continued.

Future treatments

Monoclonal antibodies that target the immune response and inflammation cascade are currently being investigated for eosinophilic oesophagitis. These include drugs that are approved for other atopic conditions, such as dupilumab, benralizumab and etrasimod.[32-35] While early data are promising, further research is required to establish the efficacy and safety of these drugs specifically for eosinophilic oesophagitis.

Management of food bolus impaction

Initial management of food bolus impaction includes clinical assessment to rule out perforation and exclude cervical surgical emphysema. Urgent upper endoscopy should be arranged with anaesthetic support for airway protection. Careful endoscopic extraction should be performed, and ideally oesophageal biopsies should be obtained above and below the site of impaction. Suction cap–assisted bolus removal improves safety and efficacy of extraction.[36]

Antispasmodics, muscle relaxants, glucagon and soft drinks have no role in the management of food bolus impaction due to eosinophilic oesophagitis.[14]

Management of fibrostenotic oesophageal strictures

In patients with advanced eosinophilic oesophagitis with oesophageal remodelling and the development of narrow-calibre oesophagus and dominant strictures, endoscopic intervention may be required. Specific dilatation techniques, such as Savory-Gilliard dilators and through-the-scope dilators, have been shown to be effective.[37] Concomitant medical therapy is advised as histological remission reduces the number of subsequent dilatations required.[38]

Data are emerging on the use of budesonide for strictures without the need for endoscopic intervention.[39]

Conclusion

Management of eosinophilic oesophagitis should be tailored to the individual patient. Dietary interventions continue to have an important role, but pharmacological options with acceptable efficacy in inducing and maintaining remission have given patients flexibility in treatment approaches. Close collaboration between gastroenterologists, immunologists, dietitians, general practitioners and pharmacists is essential for optimising treatment outcomes in eosinophilic oesophagitis. <

Conflicts of interest: Varan Perananthan is a Clinical pharmacology trainee participant on the Australian Prescriber Editorial Executive Committee (2023–24). He was excluded from editorial decision-making related to the acceptance and publication of this article.

REFERENCES

1. Navarro P, Arias A, Arias-Gonzalez 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;49:1116-25. https://doi.org/10.1111/apt.15231
2. Gonsalves N, Yang GY, Doerfler B, Ritz S, Ditto AM, Hirano I. Elimination diet effectively treats eosinophilic esophagitis in adults; food reintroduction identifies causative factors. Gastroenterology 2012;142:1451-9 e1; quiz e14-5. https://doi.org/10.1053/j.gastro.2012.03.001
3. Fitzpatrick J, Melton SL, Burgell RE. Dietary management of eosinophilic oesophagitis. Med J Aust 2023;219:340-3. https://doi.org/10.5694/mja2.52101
4. Philpott H, Nandurkar S, Thien F, Gibson PR, Royce SG. Eosinophilic esophagitis: a clinicopathological review. Pharmacol Ther 2015;146:12-22. https://doi.org/10.1016/j.pharmthera.2014.09.001
5. Hirano I, Moy N, Heckman MG, Thomas CS, Gonsalves N, Achem SR. Endoscopic assessment of the oesophageal features of eosinophilic oesophagitis: validation of a novel classification and grading system. Gut 2013;62:489-95. https://doi.org/10.1136/gutjnl-2011-301817
6. El-Serag HB, Sweet S, Winchester CC, Dent J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut 2014;63:871-80. https://doi.org/10.1136/gutjnl-2012-304269
7. Muir A, Falk GW. Eosinophilic Esophagitis: A Review. JAMA 2021;326:1310-8. https://doi.org/10.1001/jama.2021.14920
8. Maradey-Romero C, Prakash R, Lewis S, Perzynski A, Fass R. The 2011-2014 prevalence of eosinophilic oesophagitis in the elderly amongst 10 million patients in the United States. Aliment Pharmacol Ther 2015;41:1016-22. https://doi.org/10.1111/apt.13171
9. Alexander ES, Martin LJ, Collins MH, Kottyan LC, Sucharew H, He H, et al. Twin and family studies reveal strong environmental and weaker genetic cues explaining heritability of eosinophilic esophagitis. J Allergy Clin Immunol 2014;134:1084-92 e1. https://doi.org/10.1016/j.jaci.2014.07.021
10. Dellon ES, Gibbs WB, Fritchie KJ, Rubinas TC, Wilson LA, Woosley JT, et al. Clinical, endoscopic, and histologic findings distinguish eosinophilic esophagitis from gastroesophageal reflux disease. Clin Gastroenterol Hepatol 2009;7:1305-13; quiz 261. https://doi.org/10.1016/j.cgh.2009.08.030
11. Hiremath GS, Hameed F, Pacheco A, Olive A, Davis CM, Shulman RJ. Esophageal Food Impaction and Eosinophilic Esophagitis: A Retrospective Study, Systematic Review, and Meta-Analysis. Dig Dis Sci 2015;60:3181-93. https://doi.org/10.1007/s10620-015-3723-8
12. Liacouras CA, Furuta GT, Hirano I, Atkins D, Attwood SE, Bonis PA, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. J Allergy Clin Immunol 2011;128:3-20 e6; quiz 1-2. https://doi.org/10.1016/j.jaci.2011.02.040

13. Straumann A, Aceves SS, Blanchard C, Collins MH, Furuta GT, Hirano I, et al. Pediatric and adult eosinophilic esophagitis: similarities and differences. Allergy 2012;67:477-90. https://doi.org/10.1111/j.1398-9995.2012.02787.x
14. Attwood S, Epstein J. Eosinophilic oesophagitis: recent advances and practical management. Frontline Gastroenterol 2021;12:644-9. https://doi.org/10.1136/flgastro-2019-101313
15. Dellon ES, Liacouras CA, Molina-Infante J, Furuta GT, Spergel JM, Zevit N, et al. Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference. Gastroenterology 2018;155:1022-33 e10. https://doi.org/10.1053/j.gastro.2018.07.009
16. Goldin AH, Muftah M, Mangla S, Hornick JL, Hsu Blatman K, Hamilton MJ, et al. Assessment of the clinical and allergy profiles of PPI responsive and non-responsive eosinophilic esophagitis. Dis Esophagus 2023;36. https://doi.org/10.1093/dote/doac098
17. Philpott H, Nandurkar S, Royce SG, Thien F, Gibson PR. Allergy tests do not predict food triggers in adult patients with eosinophilic oesophagitis. A comprehensive prospective study using five modalities. Aliment Pharmacol Ther 2016;44:223-33. https://doi.org/10.1111/apt.13676
18. Nielsen JA, Lager DJ, Lewin M, Rendon G, Roberts CA. The optimal number of biopsy fragments to establish a morphologic diagnosis of eosinophilic esophagitis. Am J Gastroenterol 2014;109:515-20. https://doi.org/10.1038/ajg.2013.463
19. Aceves SS, Alexander JA, Baron TH, Bredenoord AJ, Day L, Dellon ES, et al. Endoscopic approach to eosinophilic esophagitis: American Society for Gastrointestinal Endoscopy Consensus Conference. Gastrointest Endosc 2022;96:576-92 e1. https://doi.org/10.1016/j.gie.2022.05.013
20. Molina-Infante J, Arias A, Alcedo J, Garcia-Romero R, Casabona-Frances S, Prieto-Garcia A, et al. Step-up empiric elimination diet for pediatric and adult eosinophilic esophagitis: The 2-4-6 study. J Allergy Clin Immunol 2018;141:1365-72. https://doi.org/10.1016/j.jaci.2017.08.038
21. Arias A, Gonzalez-Cervera J, Tenias JM, Lucendo AJ. Efficacy of dietary interventions for inducing histologic remission in patients with eosinophilic esophagitis: a systematic review and meta-analysis. Gastroenterology 2014;146:1639-48. https://doi.org/10.1053/j.gastro.2014.02.006
22. Rank MA, Sharaf RN, Furuta GT, Aceves SS, Greenhawt M, Spergel JM, et al. Technical review on the management of eosinophilic esophagitis: a report from the AGA institute and the joint task force on allergy-immunology practice parameters. Ann Allergy Asthma Immunol 2020;124:424-40 e17. https://doi.org/10.1016/j.anai.2020.03.021
23. Dellon ES, Woosley JT, Arrington A, McGee SJ, Covington J, Moist SE, et al. Efficacy of Budesonide vs Fluticasone for Initial Treatment of Eosinophilic Esophagitis in a Randomized Controlled Trial. Gastroenterology 2019;157:65-73 e5. https://doi.org/10.1053/j.gastro.2019.03.014
24. Lucendo AJ, Miehlke S, Schlag C, Vieth M, von Arnim U, Molina-Infante J, et al. Efficacy of Budesonide Orodispersible Tablets as Induction Therapy for Eosinophilic Esophagitis in a Randomized Placebo-Controlled Trial. Gastroenterology 2019;157:74-86 e15. https://doi.org/10.1053/j.gastro.2019.03.025
25. Miehlke S, Lucendo AJ, Straumann A, Jan Bredenoord A, Attwood S. Orodispersible budesonide tablets for the treatment of eosinophilic esophagitis: a review of the latest evidence. Therap Adv Gastroenterol 2020;13:1756284820927282. https://doi.org/10.1177/1756284820927282
26. Straumann A, Lucendo AJ, Miehlke S, Vieth M, Schlag C, Biedermann L, et al. Budesonide Orodispersible Tablets Maintain Remission in a Randomized, Placebo-Controlled Trial of Patients With Eosinophilic Esophagitis. Gastroenterology 2020;159:1672-85 e5. https://doi.org/10.1053/j.gastro.2020.07.039
27. Miehlke S, Schlag C, Lucendo AJ, Biedermann L, Vaquero CS, Schmoecker C, et al. Budesonide orodispersible tablets for induction of remission in patients with active eosinophilic oesophagitis: A 6-week open-label trial of the EOS-2 Programme. United European Gastroenterol J 2022;10:330-43. https://doi.org/10.1002/ueg2.12220
28. Rokkas T, Niv Y, Malfertheiner P. A Network Meta-Analysis of Randomized Controlled Trials on the Treatment of Eosinophilic Esophagitis in Adults and Children. J Clin Gastroenterol 2021;55:400-10. https://doi.org/10.1097/MCG.0000000000001356
29. Wen T, Dellon ES, Moawad FJ, Furuta GT, Aceves SS, Rothenberg ME. Transcriptome analysis of proton pump inhibitor-responsive esophageal eosinophilia reveals proton pump inhibitor-reversible allergic inflammation. J Allergy Clin Immunol 2015;135:187-97. https://doi.org/10.1016/j.jaci.2014.08.043
30. Cheng E, Zhang X, Wilson KS, Wang DH, Park JY, Huo X, et al. JAK-STAT6 Pathway Inhibitors Block Eotaxin-3 Secretion by Epithelial Cells and Fibroblasts from Esophageal Eosinophilia Patients: Promising Agents to Improve Inflammation and Prevent Fibrosis in EoE. PLoS One 2016;11:e0157376. https://doi.org/10.1371/journal.pone.0157376
31. Lucendo AJ, Arias A, Molina-Infante J. Efficacy of Proton Pump Inhibitor Drugs for Inducing Clinical and Histologic Remission in Patients With Symptomatic Esophageal Eosinophilia: A Systematic Review and Meta-Analysis. Clin Gastroenterol Hepatol 2016;14:13-22 e1. https://doi.org/10.1016/j.cgh.2015.07.041
32. Dellon ES, Rothenberg ME, Collins MH, Hirano I, Chehade M, Bredenoord AJ, et al. Dupilumab in Adults and Adolescents with Eosinophilic Esophagitis. N Engl J Med 2022;387:2317-30. https://doi.org/10.1056/NEJMoa2205982
33. Hirano I, Dellon ES, Hamilton JD, Collins MH, Peterson K, Chehade M, et al. Efficacy of Dupilumab in a Phase 2 Randomized Trial of Adults With Active Eosinophilic Esophagitis. Gastroenterology 2020;158:111-22 e10. https://doi.org/10.1053/j.gastro.2019.09.042
34. Meek PD, Hemstreet B. Emerging therapies for eosinophilic esophagitis. Pharmacotherapy 2023;43:338-48. https://doi.org/10.1002/phar.2783
35. Huguenot M, Bruhm AC, Essig M. Histological remission of eosinophilic esophagitis under asthma therapy with IL-5 receptor monoclonal antibody: A case report. World J Clin Cases 2022;10:4502-8. https://doi.org/10.12998/wjcc.v10.i14.4502
36. Ooi M, Duong T, Holman R, Huynh D, Lafta A, Grimpen F, et al. Comparison of Cap-Assisted vs Conventional Endoscopic Technique for Management of Food Bolus Impaction in the Esophagus: Results of a Multicenter Randomized Controlled Trial. Am J Gastroenterol 2021;116:2235-40. https://doi.org/10.14309/ajg.0000000000001484
37. Moawad FJ, Molina-Infante J, Lucendo AJ, Cantrell SE, Tmanova L, Douglas KM. Systematic review with meta-analysis: endoscopic dilation is highly effective and safe in children and adults with eosinophilic oesophagitis. Aliment Pharmacol Ther 2017;46:96-105. https://doi.org/10.1111/apt.14123
38. Runge TM, Eluri S, Woosley JT, Shaheen NJ, Dellon ES. Control of inflammation decreases the need for subsequent esophageal dilation in patients with eosinophilic esophagitis. Dis Esophagus 2017;30:1-7. https://doi.org/10.1093/dote/dox042
39. Schupack DA, Ravi K, Geno DM, Pierce K, Mara K, Katzka DA, et al. Effect of Maintenance Therapy for Eosinophilic Esophagitis on Need for Recurrent Dilation. Dig Dis Sci 2021;66:503-10. https://doi.org/10.1007/s10620-020-06192-8