REVIEW ARTICLE

EOSINOPHILIC ESOPHAGITIS. BEYOND THE DIET.

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Abstract

Eosinophilic esophagitis is a chronic, progressive, immune-mediated (Th2 antigen) disease that exclusively affects the esophagus. It is characterized histologically by intraepithelial infiltration of eosinophils (> 15 eosinophils per high-power field), leading to esophageal dysfunction, primarily manifested as dysphagia and food impaction. Initially, it is an inflammatory disease that can progress to a fibrostenotic pattern and is considered the most common cause of chronic dysphagia and esophagitis, second only to gastroesophageal reflux disease. As such, it currently represents the second most common cause of chronic esophagitis and the leading cause of dysphagia and food impaction in children and young adults, accounting for 7% of endoscopic diagnoses of esophageal symptoms.

EoE is considered an emerging disease with increasing incidence, likely due to the widespread use of upper gastrointestinal endoscopy in the evaluation of gastrointestinal pathology, alongside greater awareness and recognition of this condition by endoscopists and clinicians.

As a chronic disease that can progress to a fibrotic pattern, early detection and appropriate treatment are crucial.

In this review, we examine the current management of eosinophilic esophagitis, reviewing the latest evidence on the various treatment options. We analyze the therapeutic approach to follow based on the disease pattern, potential clinical and endoscopic follow-up for maintenance treatment, as well as the possibility of treatment discontinuation in selected cases.

Keywords: eosinophilic esophagitis, PPI, topical steroids, dupilumab, empiric diet.

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Introduction

Eosinophilic esophagitis (EoE) is a chronic inflammatory disease of the esophagus characterized by eosinophilic infiltration of the esophageal mucosa. Since its initial description, EoE has been the subject of increasing clinical and scientific interest, given its increasing prevalence and the complexity of its management. Understanding the evolution of the disease is fundamental to establish an adequate therapeutic approach, since it can evolve to more severe forms (fibrostenotic pattern) if it is not diagnosed early and adequate treatment is not established..

The management of EoE has evolved significantly in recent years, reflecting a better understanding of the pathogenesis of the disease and its impact on patients' quality of life. Current lines of treatment focus on addressing both esophageal inflammation and associated symptoms, and may include dietary strategies, pharmacological and, in some cases, endoscopic interventions. In addition, new therapeutic options, including biologic treatments, are being explored that promise to improve outcomes in patients with more severe forms of the disease. The decision to initiate one line of treatment or another, always using it in monotherapy, will depend on the pattern of the disease and on the decision agreed with the patient after informing him/her of the different treatment options available, the main objective of the treatment being to induce and maintain clinical and histological remission of the disease..

Therapeutic approach

Currently, several therapeutic alternatives are available for the management of EoE, aimed at controlling inflammation (by means of pharmacological or dietary treatments) and managing fibrosis and stenosis (by means of endoscopic intervention). It is possible to combine endoscopic dilatation with anti-inflammatory treatment; however, the latter will always be administered in monotherapy.

The therapeutic strategy is defined according to the two main patterns of the disease: inflammatory and fibrostenotic.

Inflammatory pattern

This pattern is characterized by inflammatory signs with or without the presence of incipient esophageal rings. In these cases, four therapeutic options are available as first-line treatments: proton pump inhibitors (PPIs), topical corticosteroids, food elimination diets and biological treatment with dupilumab (indicated as first-line only in cases of concomitance with other poorly controlled Th2-mediated disease).

The choice of treatment will depend on the availability and specific characteristics of the patient, and should be agreed with the patient. If the initial treatment is not effective (both clinically and histologically), it should be discontinued and another option should be tried until a favorable response is obtained. For patients refractory to PPIs, elimination diets and topical corticosteroids, the only alternative currently available is dupilumab.

Fibrostenotic pattern

In this pattern, initial treatment will focus on controlling inflammation with topical corticosteroids. Subsequently, endoscopic management will be carried out by progressive dilatations. In cases of refractoriness, the use of dupilumab will be indicated, accompanied by endoscopic treatment as needed.

Proton pump inhibitors (PPIs)

Over the last decade, the use of PPIs in EoE has evolved significantly from being a diagnostic tool to differentiate EoE from gastroesophageal reflux disease to being considered a therapeutic option in this pathology. This transition was the result of the International Consensus Conference for Diagnostic Criteria for EoE: Appraisal of Guidelines for Research and Evaluation II (AGREE), which supports PPI therapy for EoE in children and adults[1].

Several studies have demonstrated the efficacy of PPIs in reducing eosinophilic inflammation in patients with EoE. In a meta-analysis by Molina-Infante and Lucendo (2017), it was evidenced that more than 50 % of patients treated with PPIs presented a significant decrease in the eosinophil count in the esophageal mucosa. Additionally, improvement of symptoms, such as dysphagia, has been reported in multiple randomized clinical trials[2].

Another significant study evaluating its efficacy is the European EoE CONNECT registry[3]. This registry collects clinical, environmental and genetic data from patients with EoE, facilitating multicenter research on this disease. A recent analysis evaluated the efficacy of PPIs in a cohort of 630 patients with EoE. The results indicated that 48% of patients treated with PPIs achieved histologic remission (< 15 eos/CGA) and 71% found improvement in their symptoms. They also found

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no significant difference in efficacy between the different types of PPIs when administered at equivalent doses.

These findings support the use of PPIs as an effective therapeutic option in approximately half of the patients with EoE. In the future, the identification of factors predictive of response to PPI could optimize the selection of patients for this treatment, improving clinical and histologic outcomes.

Mechanism of action

The mechanisms by which PPIs work to reduce eosinophilia in EoE have been the subject of considerable debate and research effort[1,4]. Proposed mechanisms include PPI-induced gastric acid suppression leading to a restoration of esophageal barrier function and, on the other hand, a direct anti-inflammatory effect, inhibiting the production of proinflammatory cytokines such as interleukin 4 (IL-4), interleukin 5 (IL-5), and most prominently IL-13[5].

IL-13 plays a crucial role in the pathogenesis of EoE, since it promotes the expression of eotaxin-3, a chemokine responsible for the recruitment of eosinophils to the esophageal mucosa. This anti-inflammatory action is achieved by acting at 4 levels[6]: blocking the expression of cell surface adhesion molecules, inhibiting the migration of inflammatory cells to the esophageal epithelium; blocking STAT6-mediated eotaxin-3 (transcription factor) expression, reducing eosinophil recruitment to the esophageal epithelium; stimulation of the aryl hydrocarbon receptor, normalizing the expression of genes involved in barrier function, including filaggrin, loricrin and involucrin, through inhibition of the IL-4/IL-13-STAT6 pathway; and inhibition of ATP12A, non-gastric H-type P2, K-ATPase activity. IL-4-mediated induction of eotaxin-3 secretion is sensitive to ATP12A inhibition.

What dose of PPIs do we use to induce remission?

According to clinical guidelines, standard PPI therapy for EoE would be the standard twice-daily dose of either PPI[7]; however, there are limited data directly comparing PPI dose combinations for the treatment of EoE.

In a recent study involving a total of 305 patients with EoE, various doses of PPIs were evaluated for at least 8 weeks[8]. They found that the twice-daily prescribed PPI dose induced higher histologic response rates compared with the once-daily PPI dose, even when the total daily dose was equivalent. Histological response rates were higher with the twice-daily dosing regimen (moderate 52.8 % / high 54.3 %) compared to once-daily (standard 11.8 % / moderate 10 %) ($P < 0.0001$). In addition, double-dose treatment (40 mg omeprazole twice daily) did not appear to provide additional benefit over the moderate twice-daily dose (20 mg twice daily).

Therefore, based on the results of this study, the standard twice-daily PPI dose (20 mg omeprazole twice daily or equivalent) may be the optimal PPI regimen for inducing remission in EoE.

How long should one treat with PPIs to induce remission?

According to the recommendation of clinical practice guidelines, PPI treatment should be maintained for a minimum of 8 weeks before endoscopic evaluation[7]. However, a more recent study compiling data on the efficacy of PPIs from the multicenter EoE CONNECT database examines whether the duration of PPI treatment influences the effectiveness in achieving clinical-histologic remission of EoE[3]. The results they obtained show that PPI treatment duration of 8 to 10 weeks (56-70 days) provides a remission rate of 50.4 %; by prolonging treatment between 71 and 90 days (10 to 12 weeks), the remission rate increases to 65.2 %; however, treatment beyond the third month (>90 days) decreases effectiveness to 44.1 %, possibly due to lower patient adherence. Therefore, according to the results obtained in this study, we could consider that treatment duration of up to 12 weeks correlates with a higher probability of inducing EoE remission compared to treatments shorter than 10 weeks.

Food elimination diet

History and evolution of dietary treatment of EoE

The first study employing dietary treatment in patients with EoE was published in 1995 by Kelly [10]. In this study, 10 children were treated with an elemental diet, achieving complete histologic remission in 8 of them and clinico-histologic improvement in the remaining 2. These findings demonstrated that EoE is caused by a food allergy.

Eleven years later, in 2006, the first study on the empirical six-food elimination diet was published, showing somewhat lower response rates than the elemental diet, but reaching 74%[11]. Since then, numerous studies have confirmed the effectiveness of this dietary strategy in the treatment of EoE.

The six-food elimination diet is the most studied and has demonstrated the highest response rates[12]. However, it is a highly restrictive diet that requires a prolonged diagnostic period (at least 42 weeks) and the performance of up to seven

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Diet	Eliminated food	Response rate (%)	Pros	Cons
Elimination 6 foods	Animal milk Wheat Egg Soybeans* (legumes) Nuts Fish/Seafood	40-73	- Best studied diet - Best remission rate of the elimination diets.	- Most restrictive elimination diet. - Higher number of endoscopies. - Higher cost. - Lower adherence.
Elimination 4 foods	Animal milk Wheat Egg Soy* (legumes)	41-60	- Less restrictive. - More varied diet. - Shortened diagnostic process	- Possible lower rate of remission. - Higher cost. - Lower adherence.
Elimination 2 food	Animal milk Wheat	43	- Even less restrictive. - Avoids unnecessary restrictions. - Diagnostic process shortened. - Less impact on quality of life.	-Possible lower rate of remission.
Elimination 1 food	Animal milk	34-65	- Least restrictive diet. - Avoids unnecessary restrictions. - Shortened diagnostic process. - Fewer endoscopies. - Less impact on quality of life.	Possible lower remission rate.

Table 1. ***Empirical elimination diets. Adapted from Chang JW, Kliewer K, Haller E, Lynett A, Doerfler B, Katzka DA, et al. Development of a practical guide to implement and monitor diet therapy for eosinophilic esophagitis. Clin Gastroenterol Hepatol. 2023 Jul;21(7):1690–8.***

gastroscopies. Therefore, less restrictive alternatives have been developed, such as four-food, two-food, and single-food elimination diets (Table 1).

In 2018, Molina-Infante proposed the Step-Up strategy for diagnosis and treatment by empiric diet in patients with EoE. This strategy starts with a two-food elimination diet and, in case of no response, is progressively increased to four and six foods[13].

Protocol for the dietary management of EoE [12]

Once treatment is initiated with the elimination diet agreed with the patient, a gastroscopy with biopsies will be performed at 6-8 weeks. In case of lack of response (no histological remission), a more restrictive diet or a change to pharmacological treatment will be considered. Otherwise, food will be reintroduced, starting from the least allergenic (fish and seafood) to the most allergenic (milk of animal origin). After the reintroduction of the first food, a new gastroscopy will be performed after 4-6 weeks. If histological remission persists, the next food will be added, with endoscopic control at 4-6 weeks. In case of recurrence of the eosinophilic infiltrate after the introduction of a food, it will be identified as a trigger and definitively withdrawn. After a washout period of 4-6 weeks, another food will be introduced. This cycle will be repeated until all foods initially eliminated have been evaluated. Definitive treatment will consist of permanent exclusion of the food(s) identified as triggering the disease.

Food elimination diets based on allergy tests

Food elimination diets based on allergy tests (such as skin prick test, patch test or serum Ig test) have shown lower efficacy compared to empirical diets, as evidenced by three meta-analyses[14-16]. Currently, these tests are not recommended, as mentioned in the latest published guideline on EoE[17]. This is because these tests detect IgE-mediated allergies, whereas EoE is a lymphocyte-mediated type 2 immunity disorder characterized by delayed hypersensitivity, in which IgE does not play a relevant role. In those patients with suspected IgE-mediated food allergy, as well as before the reintroduction of food after a long period of dietary restriction, an evaluation by Allergology will be necessary, especially in children, because cases of severe immediate reactions, such as anaphylaxis, have been documented.

Topical corticosteroids

Effectiveness of topical corticosteroids in EoE

Topical corticosteroids, such as budesonide and fluticasone, have been shown to be highly effective in the

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treatment of EoE through numerous prospective, retrospective studies and up to 13 randomized, double-blind, placebo-controlled clinical trials in adults and children[18-23]. Its mechanism of action is based on the reduction of esophageal inflammation mediated by eosinophils and other inflammatory mediators through inhibition of proinflammatory cytokines, reduction of the production of key interleukins in Th2 inflammation (IL-4, IL-5 and IL-13), which promote eosinophil activation and survival; modulation of transcription factors that inhibit nuclear factor kappa B (NF-κB) and activator protein-1 (AP-1), responsible for the transcription of proinflammatory genes; reduction of eosinophilic chemotaxis (they decrease the expression of eotaxin-3, a chemokine essential for the recruitment of eosinophils to esophageal tissue); induction of eosinophil apoptosis; inhibition of Th2 differentiation; and enhancement of the epithelial barrier, promoting tissue repair, which contributes to reducing chronic damage and progression to fibrostenosis. These molecular and histological actions are essential to control chronic inflammation and prevent complications arising from fibrosis in disease progression[24].

Different formulations have been used for the treatment of EoE with topical corticosteroids (Table 2), initially with devices designed for the treatment of other organs such as inhalation devices or nasal drops. Subsequently, budesonide or viscous fluticasone preparations have been used, and are still used today, either magistral formulas prepared by pharmacists or home-made solutions. Recently, budesonide orodispersible tablets have been developed, which have shown clinical, endoscopic and histologic response rates above 95%[18]. Similar formulations of fluticasone are in phase 3 development. A recent study showed that switching to orodispersible tablets improves quality of life, treatment satisfaction, and histologic outcomes (<15 eosinophils/CGA and even <6 eosinophils/CGA), as well as endoscopic response [25].

In addition, topical corticosteroids have been shown to be more effective than PPIs and diets in both first- and second-line treatments[26]. They also achieve high long-term histologic response maintenance rates of greater than 60%, with excellent treatment adherence and low rate of adverse effects[27].

According to data from the European EoE CONNECT registry[26], fluticasone is used more frequently than budesonide (6:4 ratio). Nasal drops are the most common presentation of fluticasone, whereas for budesonide master formulations predominate, followed by orodispersible tablets. The analysis also showed that budesonide is more effective than fluticasone, budesonide orodispersible tablets are more effective than other formulations, high doses (2 mg budesonide, 0.8 mg fluticasone) are more effective than low doses, and that the severity of symptoms is inversely proportional to the response to topical corticosteroid treatment.

Adverse effects[5]

Topical corticosteroids are safe in the long term, as evidenced by a study of nearly 1,000 patients, where adverse effects were mainly mild to moderate[28]. The most common was oral and esophageal candidiasis, frequently asymptomatic and rarely requiring discontinuation of treatment. Its management includes topical (clotrimazole) or systemic (fluconazole) antifungal agents, dose reduction or temporary suspension in severe cases. Adrenal insufficiency is a rare complication. Although adrenal function monitoring is not required in short treatments, it could be considered in prolonged therapies.

Biologic treatment. Dupilumab.

Dupilumab is the first biologic drug approved for EoE. Its indications would be: adult and adolescent patients aged 12 years and older, weighing at least 40 kg, who are inadequately controlled, intolerant or not candidates for conventional drug therapy. The recommended dose is 300 mg every week, administered by subcutaneous injection[29-30].

It is a recombinant human IgG4 monoclonal antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling through the type I receptor (IL-4Rα/γc) and type II receptor (IL-4Rα/IL-13Rα). IL-4 and IL-13 are the main drivers in type 2 inflammation present in diseases such as atopic dermatitis, asthma or EoE. Blockade of the IL-4/IL-13 pathway by dupilumab interrupts a critical pathway in the inflammatory response observed in the esophageal epithelium in patients with EoE.

Efficacy

The evaluation of the efficacy of dupilumab in EoE is based on a randomized, double-blind, multicenter, placebo-controlled, phase 3 clinical trial[31]. The study consisted of 3 parts: A, B, and C. Parts A and B each consisted of a 24-week double-blind treatment period. After this treatment period, patients in parts A and B had the option to enter part C, which consisted of a 28-week treatment extension period, the objective of which was to evaluate safety and efficacy up to 52 weeks of treatment with dupilumab. The results they obtained were that the proportion of patients achieving histological deep remission < 6 eos/CGA was significantly higher in patients treated with dupilumab, regardless of receiving dupilumab weekly or every 2 weeks versus the placebo group.

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	Formulation	Doses	Remission rates
Fluticasone 59%	nasal drops 74%	0,8 mg/day 68,7%	66,2%
		0,4 mg/day 12%	29,6%
Budesonide 41%	compounded formula 57,4%	2 mg/day 68,7%	80,2%
		1 mg/day 6,5%	63,6%
	orodispersible tablet 26%	2 mg/day 55,7%	100%
		1 mg/day 44,3%	86,2%
	home-made 9,1%	2 mg/day 44,1%	80%
		1 mg/day 41,2%	100%
	inhaler 7,5%	2 mg/day 67,9%	93,3%
		1 mg/day 17,9%	-

Table 2. ***Use of topical corticosteroids in daily clinical practice. Data from Laserna-Mendieta EJ, Navarro P, Casabona-Francés S, Savarino EV, Amorena E, Pérez-Martínez I, et al. Swallowed topical corticosteroids for eosinophilic esophagitis: utilization and real-world efficacy from the EoE CONNECT registry. United European Gastroenterol J. 2024 Jun;12(5):585–595.***

In contrast, when analyzing clinical improvement in dysphagia, they found that patients receiving weekly dupilumab achieved greater symptom control after 4 weeks of treatment when compared with the placebo group. However, such clinical improvement was not obtained in the group of patients who were administered every 2 weeks.

Therefore, taking into account these results, and the fact that the histological remission rates are similar when prescribed weekly or every 2 weeks, the use of dupilumab could be evaluated in one way or another depending on the patient's symptoms.

Safety

Clinical trials and post-marketing studies have shown that dupilumab has a favorable safety profile in patients with EoE, similar to that observed in other indications (such as atopic dermatitis or asthma). Most of the adverse effects reported are mild to moderate, mainly injection site reactions (erythema, pain, inflammation). Among patients with EoE, the frequency of conjunctivitis was low and similar between the dupilumab or placebo group and there were no cases of keratitis[31,32].

Other emerging biologic therapies

Currently an area of intense research activity, there are a large number of biologic drugs that could be used for the treatment of EoE and other gastrointestinal eosinophilic diseases. The drawback is that we do not know the medium- and long-term efficacy and safety of the new molecules. Nor have they demonstrated the ability to modify the natural history of EoE.

These therapies target different cytokines involved in the inflammatory response in EoE. Ongoing studies of agents targeting IL-5, such as mepolizumab, reslizumab, and benralizumab should provide more information on whether targeting this pathway is feasible. It is expected that ongoing studies evaluating agents targeting other novel pathways, such as Siglec-8 (lirentelimab), IL-13 (cendakimab), sphingosine 1-phosphate receptor (etrasimod), and TSLP blocker (tezepelumab) will provide additional options for chronic management of EoE[33,34].

Endoscopic treatment: Can endoscopic dilatation be performed?

Experts recommend that adult patients with dysphagia due to stenosis associated with EoE should undergo endoscopic dilatation rather than no dilatation[35]. It should be taken into account that this is a chronic and fibrostenotic disease, which over time produces esophageal remodeling that can lead to the formation of permanent rings and changes in caliber (narrow esophagus) that will require endoscopic dilatations to resolve them. Esophageal dilatation is a mechanical procedure with no anti-inflammatory effect, aimed at widening the lumen of an esophagus of reduced caliber and leads to rapid symptomatic improvement in 95% of patients[36].

Dilatation is therefore indicated in patients with fibrous strictures or narrow-caliber esophagi that condition dysphagia

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or frequent episodes of food impaction despite effective pharmacological or dietary treatment. The American guidelines state that the ideal goal would be to reach 15-18 mm[37]. In any case, dilatation should not exceed 3 mm per session due to the risk of complications, and the ideal interval between sessions remains to be determined[38]. Balloons or rigid dilators can be used, and care should always be taken to look closely at the mucosa after removing the dilator and before increasing the caliber to detect tears. Risk factors for complications are young age, previous dilatations, upper esophageal stenosis and inability to pass with the endoscope[39]; however, complications of dilatation in EoE are rare, and although there is a risk of perforation of less than 0.4%, no mortality has been reported.

It should be kept in mind that endoscopic dilatation does not modify the underlying eosinophilic inflammation; therefore, it should not be used as the only therapeutic option for EoE, but should always be combined with effective anti-inflammatory treatment (PPI, diet, glucocorticoids or biologic therapy)[39].

Issues to be resolved in the management of the patient with EoE.

We know, therefore, that EoE is a chronic immune-mediated disease that, in the absence of treatment, presents a high probability of recurrence and can progress to structural complications, such as fibrostenosis, with the primary goal of treatment being to achieve clinical, histologic, and endoscopic remission of the disease[40].

One of the major outstanding issues in EoE is the lack of robust evidence on the efficacy and safety of long-term maintenance therapy. Currently, there are few studies designed to evaluate how to maintain clinical and histologic remission without exposing the patient to prolonged side effects or compromising treatment adherence. Furthermore, there is no consensus on the optimal time to perform revision endoscopies, either in the context of therapeutic de-escalation or during the maintenance phase[41]. Finally, doubts persist as to whether it is possible to discontinue treatment in certain patients who achieve sustained remission, and what would be the criteria for making this decision safely. These unknowns underscore the need for long-term prospective studies and more personalized approaches to disease management.

1. What is the optimal clinical and endoscopic follow-up?

The scientific evidence on the follow-up of patients with EoE is limited. However, there is a consensus document developed by North American and European experts that provides recommendations on how to perform this follow-up[42].

Monitoring in EoE seeks to determine whether the patient is improving, but this poses challenges due to the chronic nature of the disease, its recurrence upon discontinuation of treatment, and the potential loss of therapeutic efficacy over time. Long-term follow-up is required, evaluating symptoms, endoscopic and histologic findings to get a complete picture of disease activity. Symptoms, although fundamental, have limited correlation with the biological parameters of the disease. They may improve while active inflammation persists, due to avoidance behaviors or esophageal dilations, or they may persist even after controlling inflammation due to factors such as undetected strictures, esophageal hypervigilance, or feeding dysfunction. It is essential to inquire in detail about dysphagia, feeding behaviors and feeding dysfunction. The EREFS system is recommended to assess endoscopic response. Complete normalization corresponds to a score of 0, although a score ≤2 is a reasonable goal. Comparing pre- and post-treatment findings helps to assess evolution. Histologically, the goal is to achieve <15 eos/hpf (<60 eos/mm^2), so biopsies should be taken at each follow-up endoscopy.

The ideal concept of "deep resolution" combines symptom resolution and endoscopic and histologic normalization. However, it is achievable in few patients; for example, only 9.4% of patients in a Swiss study achieved this remission, and the median relapse was 22 weeks after stopping treatment. This highlights the need for continued follow-up even in patients in remission.

The follow-up interval varies according to treatment and individual characteristics. We will perform endoscopy after 8-12 weeks of starting PPIs, topical corticosteroids or elimination diet. Dupilumab requires 12-24 weeks to evaluate response. If there are no complications (impaction, perforations, malnutrition), clinical follow-up can be regular. However, a gap in care longer than 2 years increases the risk of fibrostenosis.

Although up to now biopsies are still essential, less invasive methods are being explored such as transnasal endoscopy that reduces costs and exposure to anesthesia, especially in children, cytosponge which is a capsule with a cytological brush that collects tissue when extracted; it has good tolerance and acceptable sensitivity, esophageal String Test that manages to detect inflammatory markers by absorbing them during their stay in the esophagus and other techniques such as mucosal impedance and EndoFLIP, which evaluate biomechanical and structural characteristics during endoscopies.

2. Is it possible to interrupt treatment in EoE?

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EoE is a chronic immune-mediated disease that requires continuous management to prevent persistent inflammation and structural complications, such as fibrosis and stenosis. For this reason, treatment discontinuation is a topic of debate in the scientific and clinical community, especially in patients who achieve sustained clinical and histologic remission.

Current management guidelines, such as those of the American Gastroenterological Association (AGA)[43] and the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN)[44], recommend a continuous treatment approach for most patients, given the risk of disease recurrence and progression. Several studies have evaluated the impact of withholding specific treatments, such as diet and medical treatment.

The results show that most patients experience clinical and histological relapse after discontinuation, even in those with sustained remission.

However, we believe that in certain selected cases a "suspension test" could be considered, especially in patients with mild EoE (no fibrostenotic pattern) and those who have maintained clinical and histologic remission for a prolonged period (>12 months). In these scenarios, discontinuation should be performed with close follow-up with periodic clinical and endoscopic evaluation to detect early relapses. This decision to discontinue treatment should be based on an individualized assessment that considers disease activity, risk of complications, and patient preferences. Future studies will help to better define patient subgroups that could benefit from therapeutic de-escalation strategies.

Conclusions and areas for improvement

EoE is a chronic and progressive disease[40]. These inherent characteristics of the disease have several practical consequences. First, once diagnosed, EoE requires a long-term management strategy. Second, maintenance treatment should be continued after achieving clinico-histologic remission. Third, patients with ongoing treatment need to have regularly scheduled clinical follow-up to assess for disease-related adverse events and side effects of medications or diets. Fourth, because the absence of symptoms is not a guarantee of endoscopic or histologic remission, periodic assessment of inflammatory activity by endoscopy and biopsy should be considered. There is little data to guide the frequency of clinical and endoscopic evaluations, although expert opinion dictates that at least once a year a complete evaluation should be done.

Regarding the possibility of discontinuing treatment, this remains a challenge, as most patients require long-term maintenance treatment to avoid relapses and complications, such as esophageal stricture. Although some patients with mild disease who manage to maintain a sustained histologic remission may be candidates for stopping treatment, most of them should be closely monitored to prevent disease recurrence.

Considering the natural history of the disease, there are several areas that could be improved to optimize the management of EoE. First, the identification of specific biomarkers that can predict relapses and allow more precise treatment personalization. Second, further studies on treatment discontinuation are essential to more clearly define clinical criteria and strategies for safe medication tapering. In addition, research on the long-term impact of current therapies on remission and relapse is essential to improve disease management.

In summary, treatment of EoE requires an individualized approach, rigorous monitoring and continuous assessment of therapeutic response. In the future, further studies will be needed to expand knowledge on the efficacy and long-term effects of therapies, which would allow the management of this chronic disease to be optimized.

Bibliography

1. *Dellon ES, Liacouras CA. International Consensus Guidelines for Diagnosis and Management of Eosinophilic Esophagitis: AGREE Conference Recommendations. Gastroenterology. 2018;154(2):292–309.*

2. *Molina-Infante J, Lucendo AJ. Meta-analysis on proton pump inhibitors in eosinophilic esophagitis: Effectiveness and safety. J Allergy Clin Immunol. 2017;140(6):1731–42.*

3. *Dellon ES, Hirano I. Eosinophilic esophagitis: pathogenesis and management. Clin Rev Allergy Immunol. 2018;55(1):70–84.*

4. *Laserna-Mendieta EJ, Casabona-Frances S, Guagnozzi D, et al. European Registry on Eosinophilic Esophagitis (EoE CONNECT): Analysis of treatment patterns and remission rates. Aliment Pharmacol Ther. 2020;52(8):1410–20.*

5. *Lucendo AJ. Eosinophilic esophagitis: Proton pump inhibitors as a therapeutic option beyond acid suppression. Curr Opin Gastroenterol. 2013;29(4):419–25.*

DOI: 10.37352/2025482.3

6. Franciosi JP, Veerappan GR, Guider J, et al. Proton pump inhibitors in eosinophilic esophagitis: Cytokine modulation and effects on eotaxin-3. Gastroenterol Res Pract. 2022;2022:9708932.

7. Muftah S, Thompson J, Smith E, et al. Dose-dependent response of proton pump inhibitors in eosinophilic esophagitis: Results from a multicenter cohort. Clin Gastroenterol Hepatol. 2024;22(1):33–40.

8. Lucendo AJ, Molina-Infante J, Arias Á, et al. Guidelines for management of eosinophilic esophagitis in children and adults. United European Gastroenterol J. 2017;5(3):335–58.

9. Laserna-Mendieta EJ, Casabona-Frances S, Guagnozzi D, et al. Effectiveness of proton pump inhibitors and treatment duration in eosinophilic esophagitis: Data from the EoE CONNECT registry. Aliment Pharmacol Ther. 2020;52(8):1245–54.

10. Kelly K. Treatment of eosinophilic esophagitis with an elemental diet. Gastroenterology. 1995;108(3): 793-796.

11. Kagalwalla AF, Sentongo TA, Li BU, et al. Effect of six-food elimination diet on clinical and histologic outcomes in eosinophilic esophagitis. Clinical Gastroenterology and Hepatology. 2006;4(9): 1097-1102.

12. Chang J, Dods D, Vasilenko E, et al. Six-food elimination diet in eosinophilic esophagitis. Clin Gastroenterol Hepatol. 2023;21(3): 456-463.

13. Molina-Infante J, et al. Step-Up strategy in the treatment of eosinophilic esophagitis. J Allergy Clin Immunol. 2018;142(5): 1576-1584.

14. Molina-Infante J, et al. Systematic review of allergy tests in eosinophilic esophagitis. Revisión sistemática. 2018.

15. Reed CC, et al. Allergy tests in eosinophilic esophagitis: meta-analysis results. Revisión sistemática. 2020.

16. Pitsios C, et al. Diet and allergy testing in eosinophilic esophagitis. J Clin Med. 2022;11(5): 1351.

17. Dellon ES, et al. New guidelines for managing eosinophilic esophagitis. Am J Gastroenterol. 2025;120(3): 555-567.

18. Lucendo AJ, et al. Topical corticosteroids in eosinophilic esophagitis: results of 13 randomized controlled trials. Gastroenterology. 2019;157(4): 974-986.

19. Hirano I, et al. Topical steroids for eosinophilic esophagitis: efficacy and safety. Clin Gastroenterol Hepatol. 2022;20(7): 1509-1519.

20. Dellon ES, et al. Topical corticosteroids in the treatment of eosinophilic esophagitis: a review. Gastroenterology. 2017;153(2): 416-425.

21. Miehlke S, et al. The role of corticosteroids in eosinophilic esophagitis. Gut. 2016;65(10): 1564-1570.

22. Hirano I, et al. The efficacy of topical corticosteroids for eosinophilic esophagitis. Gastroenterology. 2020;159(4): 1084-1091.

23. Dellon ES, et al. Corticosteroids in eosinophilic esophagitis: a clinical review. Clin Gastroenterol Hepatol. 2022;19(3): 551-564.

24. Dellon ES, Hirano I. Molecular and histologic mechanisms of corticosteroids in eosinophilic esophagitis. Gastroenterology. 2018;154(2): 425-436.

25. Pellegatta G, et al. Efficacy of budesonide oral disintegrating tablets in eosinophilic esophagitis. Clin Gastroenterol Hepatol. 2024;22(6): 1274-1283.

26. Laserna-Mendieta EJ, et al. Corticosteroid therapies in eosinophilic esophagitis: a comparison of budesonide and fluticasona. Clin Gastroenterol Hepatol. 2020;18(2): 383-391.

27. McCallen J, et al. Long-term effectiveness and adherence to topical corticosteroids in eosinophilic esophagitis. J Clin Gastroenterol. 2024;58(2): 225-233.

28. Hirano I, et al. Safety of topical corticosteroids in eosinophilic esophagitis. Aliment Pharmacol Ther. 2023;58(7): 669-677.

29. CIMA. Dupilumab en el tratamiento de la esofagitis eosinofílica. 2024.

30. Al-Horani RA. Dupilumab: un avance en el tratamiento de la esofagitis eosinofílica. J Clin Immunol. 2022.

31. Dellon ES, Liacouras CA, Hruz P, et al. Efficacy of dupilumab in patients with eosinophilic esophagitis: a randomized, double-blind, placebo-controlled trial. N Engl J Med. 2022;387(6):501-511.

32. Rothenberg ME, van der Meer R, Erwin EA, et al. Dupilumab for the treatment of eosinophilic esophagitis: a phase 3 trial. Lancet. 2023;401(10372):1753-1762.

33. Greuter T, et al. Emerging biologic therapies in eosinophilic esophagitis. Curr Opin Gastroenterol. 2020;36(4):277-285.

DOI: 10.37352/2025482.3

34. Meek G, et al. Investigational biologic agents for eosinophilic esophagitis: a review of current progress. Expert Opin Investig Drugs. 2023;32(2):203-211.

35. Rank MA, et al. Endoscopic balloon dilation in the management of eosinophilic esophagitis. World J Gastroenterol. 2020;26(12):1404-1412.

36. Moawad FJ, et al. Endoscopic dilation for eosinophilic esophagitis: analysis of safety and efficacy. Am J Gastroenterol. 2017;112(5):812-817.

37. Hirano I, Pandolfino JE. Management of eosinophilic esophagitis: the role of endoscopic dilation. J Clin Gastroenterol. 2017;51(4):320-325.

38. Lynch SM, et al. Eosinophilic esophagitis: endoscopic management and dilation techniques. Dis Esophagus. 2020;33(1):1-8.

39. Dellon ES, et al. Endoscopic findings and treatment outcomes in eosinophilic esophagitis. Gastrointest Endosc. 2010;72(3):587-594.

40. Dellon ES. Managing eosinophilic esophagitis: an evidence-based approach. Clin Gastroenterol Hepatol. 2018;16(9):1386-1394.

41. Von Arnim U, et al. Expert consensus on the follow-up and long-term management of eosinophilic esophagitis. Clin Gastroenterol Hepatol. 2023;21(2):225-233.

42. Dellon ES, et al. Consensus recommendations on the management of eosinophilic esophagitis: treatment strategies and long-term care. J Allergy Clin Immunol. 2020;145(1):35-45.

43. Papadopoulou A, et al. Eosinophilic esophagitis in children: a guide to clinical management. Eur J Pediatr. 2017;176(6):723-731.

44. Philpott H, et al. Long-term treatment and maintenance strategies in eosinophilic esophagitis. Aliment Pharmacol Ther. 2018;47(1):72-81.

DOI: 10.37352/2025482.3