Top Three Treatments for Eosinophilic Esophagitis Dysphagia Relief

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> Eosinophilic esophagitis (EoE) is a chronic, immune-mediated esophageal disease characterised by eosinophil-predominant inflammation, leading to esophageal dysfunction and dysphagia. Effective management focuses on reducing esophageal eosinophilia and improving symptoms. The three primary treatment modalities for EoE-related dysphagia relief are proton pump inhibitors (PPIs), topical corticosteroids, and dietary elimination.1

KEY TAKEAWAYS

- The Pivot: Established treatments continue to form the cornerstone of EoE management, with ongoing refinement in their application.
- The Data: PPIs achieve histological remission in approximately 50% of adult EoE patients, while topical corticosteroids show remission rates of 70-80%.
- The Action: Clinicians should initiate treatment with PPIs, escalating to topical corticosteroids or dietary elimination if symptoms persist or histological remission is not achieved.

Eosinophilic esophagitis (EoE) presents a significant clinical challenge, with dysphagia being the most common and debilitating symptom. The underlying pathology involves an allergic inflammatory response within the esophageal mucosa, leading to fibrosis and stricture formation.1 This chronic, immune-mediated disease is characterized by the infiltration of eosinophils into the esophageal lining, which can be triggered by specific food or environmental allergens. The prevalence of EoE has been increasing globally, affecting approximately 1 in 2,000 individuals, with a higher incidence in males and Caucasians.1 Management strategies aim to control this inflammation, thereby alleviating symptoms and preventing disease progression. The current evidence supports three main therapeutic approaches: proton pump inhibitors (PPIs), topical corticosteroids, and dietary elimination.2

Pharmacological and Dietary Interventions for EoE

Proton pump inhibitors (PPIs) are often the initial therapeutic choice for EoE. While traditionally used for acid suppression, PPIs have demonstrated anti-inflammatory effects in the esophageal mucosa, independent of their acid-reducing properties.3 This anti-inflammatory action is particularly relevant in a subset of patients termed PPI-responsive esophageal eosinophilia (PPI-REE), who exhibit clinical and histological features indistinguishable from EoE but respond to PPI therapy.3 Studies indicate that PPIs can induce histological remission (defined as fewer than 15 eosinophils per high-power field) in approximately 50% of adult EoE patients.4 Symptomatic improvement, including relief from dysphagia, is observed in a similar proportion of patients. The mechanism is thought to involve

inhibition of eotaxin-3 expression and modulation of tight junction proteins, which are crucial in maintaining esophageal barrier integrity and regulating eosinophil recruitment.3 The convenience of oral administration and a favorable safety profile make PPIs an attractive first-line option, particularly for patients with co-existing gastroesophageal reflux disease (GERD) symptoms.

Topical corticosteroids, such as fluticasone propionate and budesonide, are highly effective in treating EoE. These agents are administered orally, typically as a swallowed slurry or spray, allowing direct contact with the esophageal mucosa.5 This localized delivery minimizes systemic absorption and reduces the risk of systemic corticosteroid side effects. Fluticasone propionate, delivered via a metered-dose inhaler and swallowed, has shown histological remission rates ranging from 70% to 80% in both adult and paediatric populations.6 Budesonide, often formulated as an oral viscous slurry, demonstrates similar efficacy, with remission rates also in the 70-80% range.7 Both agents significantly improve dysphagia and other EoE symptoms, such as chest pain and food impaction. The main adverse event associated with topical corticosteroids is oral candidiasis, which occurs in approximately 5-10% of patients and is typically managed with antifungal therapy without requiring discontinuation of EoE treatment.6,7

Dietary elimination therapy involves identifying and removing specific food allergens that trigger the inflammatory response in EoE. The most common approach is the six-food elimination diet (SFED), which removes milk, wheat, soy, egg, peanut/tree nuts, and fish/shellfish.8 This broad elimination diet has shown high efficacy, with histological remission rates of 70-75%.9 However, the SFED is restrictive and requires subsequent reintroduction of foods with endoscopic biopsies to identify specific triggers, which can be burdensome for patients.8 This process often involves multiple endoscopies over several months, impacting patient quality of life and adherence. A more targeted approach, such as allergy testing-directed elimination, has lower efficacy (approximately 40-50% remission) but is less restrictive, relying on skin prick tests or atopy patch tests to guide food removal.10 Elemental diets, consisting of amino acid-based formulas, are the most effective dietary therapy, achieving remission in over 90% of patients, but are generally reserved for severe cases or those unresponsive to other therapies due to their palatability and cost.11 The significant commitment required for dietary therapies, particularly SFED, necessitates strong patient education and support to ensure compliance and successful outcomes.

The choice of therapy often depends on patient preference, disease severity, and response to initial treatment. While PPIs offer a convenient first-line option, topical corticosteroids provide higher remission rates. Dietary therapy, particularly SFED, is highly effective but demands significant patient adherence and diagnostic follow-up. Combination therapies are also employed in refractory cases, where patients do not achieve adequate control with monotherapy.12 Emerging therapies, including biologics targeting specific inflammatory pathways, are also under investigation and may offer additional options for patients with difficult-to-treat EoE in the future. The long-term management of EoE often requires ongoing therapy to prevent symptom recurrence and esophageal remodeling.

> **CLINICAL IMPLICATIONS**
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> The continued reliance on PPIs, topical corticosteroids, and dietary elimination for EoE management underscores a persistent gap in novel therapeutic development. While these treatments are effective, their limitations are well-documented: PPIs only work for half of patients, topical steroids carry a candidiasis risk, and dietary elimination is notoriously difficult to sustain. Clinicians are left navigating a landscape where the

'best' option is often the one a patient can adhere to, rather than a definitively superior pharmacological agent. This situation highlights the need for more targeted, less burdensome therapies that offer higher remission rates without significant lifestyle disruption.

From an industry perspective, the market for EoE treatments remains ripe for innovation. The current therapeutic arsenal, while functional, does not fully address the unmet needs of all patients. The development of novel biologics, such as dupilumab, which recently received FDA approval for EoE, represents a significant step forward. However, the high cost and administration route of such therapies mean that the established, more affordable options will likely remain the first line for many. Pharmaceutical companies should focus not only on entirely new mechanisms but also on improving the delivery and tolerability of existing effective compounds, perhaps through novel formulations of topical steroids that minimise candidiasis risk or enhance esophageal retention.

Patients with EoE face a chronic condition requiring long-term management, often involving repeated endoscopies and biopsies to monitor disease activity. The burden of dietary elimination, particularly for children, is substantial, impacting quality of life and potentially nutritional status. The availability of multiple effective options is a strength, but the lack of a single, universally effective, and easily administered treatment means patients must often cycle through therapies or combine them. This necessitates robust patient education and shared decision-making, ensuring that the chosen treatment aligns with individual circumstances and preferences, rather than a one-size-fits-all approach. The goal should be sustained remission, not just symptomatic relief, to prevent long-term complications like strictures.

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