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REVIEW

Expert Opinion on the Management, Challenges, and Knowledge Gaps Pertaining to Eosinophilic Esophagitis Among Adults in the Greater Gulf Region

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Abstract: Eosinophilic esophagitis (EoE) is a type 2 inflammatory esophageal disease that presents in adults as dysphagia and food impaction. EoE is characterized by a predominance of T helper 2 cells among the T cell population. Environmental agents, including food antigens and aeroallergens, trigger EoE. EoE exhibits immunoglobulin E- (IgE-) and non-IgE-mediated allergic responses to these environmental allergens. Local antigen-specific IgE can also trigger mast cell degranulation, thereby worsening EoE. Individuals with atopic dermatitis, asthma, IgE-mediated food allergy, or allergic rhinitis are at a higher risk of developing EoE. EoE treatment aims to achieve clinical improvement, endoscopic mucosal healing, and reduction in or resolution of histological inflammation. However, attaining and maintaining "deep remission" with conventional treatments can be challenging, underscoring the need for targeted therapies. This expert opinion focuses on the latest global recommendations for using novel therapies to improve outcomes in patients with EoE. It also highlights current practices in the Greater Gulf region to manage EoE, identify challenges, and address future educational gaps.

Keywords: eosinophilic esophagitis, esophageal disease, dupilumab, monoclonal antibody, expert opinion, Greater Gulf

Introduction

Eosinophilic esophagitis (EoE) is an allergic/immune-mediated esophageal disorder characterized clinically by symptoms of esophageal dysfunction. Histologically, esophageal biopsies show ≥15 intraepithelial eosinophils per high-power field (HPF) in the absence of eosinophilia due to other secondary causes.[1–5] The updated international consensus diagnostic criteria for EoE define "suspected EoE" and "confirmed EoE" as symptoms of esophageal dysfunction with at least 15 eosinophils (eos)/hpf (or ~60 eos/mm^2) and at least 15 eos/hpf (or ~60 eos/mm^2) on esophageal biopsy, respectively, after evaluation for other causes of esophageal eosinophilia.[2] Over the past two decades, EoE has been recognized as a major cause of upper gastrointestinal morbidity. However, the epidemiology of EoE has also rapidly evolved. The incidence and prevalence of EoE have notably increased, outpacing the advancements in diagnostic techniques that assist in disease recognition.[1]

The incidence and prevalence of EoE range from 5 to 10 cases per 100,000 individuals and 0.5 to 1 case per 1000 individuals, respectively.[3–5] However, epidemiological data on the prevalence of EoE in the Greater Gulf region is scarce. A recent systematic review and meta-analysis reported the incidence and prevalence of EoE in 40 studies from 1976 to 2022. The pooled global incidence and prevalence of EoE were 5.31 cases per 100,000 and 40.04 cases per 100,000 inhabitant-years,

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respectively. The study reported an increase in the incidence and prevalence of EoE by 27.2 and 9.1 times, respectively, compared with those before the 2000s.[6] This article delves into the potential reasons behind this increase, scrutinizes risk factors, and pinpoints crucial areas for research on the etiology of EoE. The progression of EoE from an inflammatory to a fibrostenotic phenotype is also discussed. The natural history of EoE is essential in discussions with patients about disease prognosis and decisions on the long-term use of medicines and/or endoscopic and diet therapies. Although progressive remodeling in EoE appears gradual, it is not universal, and currently, the best predictor of stricture risk is the duration of untreated disease. Ultimately, to fully understand the natural history of EoE, more prospective, long-term outcome studies focusing on multiple aspects of this disease are required.[3–5]

EoE is caused by a combination of genetic factors, environmental allergens, and an immune response mediated by T helper 2 cytokines (interleukin [IL]-4, IL-5, and IL-13). These cytokines promote eosinophil activation and tissue remodeling, leading to EoE symptoms. Moreover, EoE includes epithelial barrier dysfunction, mast cell activation, and eosinophil degranulation, which lead to inflammation and tissue damage. Chronic inflammation can result in fibrosis, causing long-term complications such as strictures and esophageal dysfunction.[7]

The goals of EoE treatment are clinical improvement, endoscopic mucosal healing, and reduction in or resolution of histological inflammation. Nevertheless, achieving and sustaining "deep remission", defined as a complete normalization in endoscopic and histologic findings and the absence of symptoms with conventional treatments, can be difficult, thus highlighting the need for novel targeted therapies, such as biologics.[3] Typically, treatments such as topical corticosteroids —with one formulation approved by the European Medicines Agency (EMA) and another formulation approved in 2024 by the United States Food and Drug Administration (US FDA)—are available in the Greater Gulf region.[8,9] Proton pump inhibitors (PPIs; off-label use) are the mainstay pharmacologic options to reduce eosinophilic inflammation.[3,10]

In a meta-analysis of 33 studies (N=619 patients) evaluating the efficacy of PPIs for inducing histologic remission in patients with symptomatic EoE, it was observed that PPIs resulted in symptomatic improvement in 60% of patients and a histological response of 50%, with no difference between the adult and pediatric populations.[11] Diet elimination therapies are nonpharmacologic options that include empiric elimination of foods or, in some cases, an amino acid-based formula. EoE is known to be triggered by food antigens, as demonstrated by the fact that almost 90% of children and adults unresponsive to PPIs subsequently respond to an elemental diet.[4] Studies suggest that although no reliable methods exist for identifying foods that trigger EoE, the six-food elimination diet, which includes eliminating wheat, milk, nuts, soy, seafood, and eggs from the diet, is used frequently to achieve remission histologically.[12] However, restrictive diets can negatively affect a patient's quality of life (QoL) and can be challenging to adhere to in the long term.[13] Another treatment option is esophageal dilation, which is recommended for fibrostenotic complications such as esophageal strictures or narrowing.[14,15] However, symptom response to dilation can be temporary, and because dilation does not impact the underlying EoE disease activity, it needs to be paired with anti-inflammatory therapy.[16]

In 2022, the monoclonal antibody dupilumab, which targets the IL-4 receptor alpha to reduce IL-4 and IL-13 signaling, became the first therapy approved by the US FDA for EoE management.[3,9] The EMA and other regulatory authorities worldwide subsequently approved it. While progress has been made in EoE treatment, further research is needed to refine diagnostics, treatment, and follow-up, improving long-term outcomes and QoL for patients.[17]

With the growing focus on EoE treatment, this expert opinion focuses on the most recent global recommendations for using biologics and novel therapies to improve outcomes in patients with EoE. Existing practices for managing EoE in the Greater Gulf region, challenges in management, and educational gaps to be addressed in the future are also discussed.

Methods

An expert panel committee across the Greater Gulf region extensively reviewed the relevant literature available in the PubMed Central database using the keywords "eosinophilic esophagitis" OR "EoE" AND "management" AND "recommendation". Data was collected for the 5 years from May 2018 to May 2023 before the expert committee meeting. The MeSH terms mentioned in the next paragraph were generated upon the initial search on PubMed using the keywords mentioned above.

((("eosinophilic esophagitis"[MeSH Terms] OR ("eosinophilic"[All Fields] AND "esophagitis"[All Fields]) OR "eosinophilic esophagitis"[All Fields]) OR "EoE"[All Fields]) AND ("organization and administration"[MeSH Terms]

OR ("organization"[All Fields] AND "administration"[All Fields]) OR "organization and administration"[All Fields] OR "management"[All Fields] OR "disease management"[MeSH Terms] OR ("disease"[All Fields] AND "management"[All Fields]) OR "disease management"[All Fields])) AND recommendations[All Fields] AND ("2018/01/01"[PubDate]: "2023/05/25"[PubDate]).

Following the initial title and abstract screening on PubMed, an advanced search across other electronic databases, including MEDLINE, Embase, CINAHL, Web of Science, Scopus, and Google Scholar, was performed to identify additional literature relevant to the study.

Following the comprehensive literature search and understanding of the knowledge gaps, an expert advisory meeting was conducted to address EoE management and its recommendations across the Greater Gulf region. The session was led by a prominent expert and featured a panel of specialists from various areas of the Greater Gulf. All expert opinion statements were formulated during the meeting based on the physicians' prior knowledge of the subject, and a comprehensive literature search was conducted beforehand.

The objective of the meeting was to:

- Gain insights into the current EoE management implemented across the Greater Gulf region and challenges within current practices
- Discuss the newly published global recommendations
- Gain insights into global EoE management recommendations' applicability in the current clinical practice
- Propose recommendations for the ideal treatment algorithm in the Greater Gulf region
- Propose educational gaps to be addressed in the future

Current EoE Management and Challenges Associated with the Existing Practices in the Greater Gulf Region

Treatment strategies for EoE include dietary modifications, pharmaceutical interventions, and esophageal dilation to achieve clinical, histological, and endoscopic remission; prevent complications associated with tissue remodeling and nutritional deficiencies; address symptoms of esophageal dysfunction; and ensure a satisfactory health-related QoL.[18,19]

Dietary Modifications

The American Gastroenterological Association (AGA), the Joint Task Force (JTF) on Allergy-Immunology Practice Parameters, and the British Society of Gastroenterology recommend the use of an elemental diet and an empiric six-food, four-food, and two-food elimination diet based on the patient's age and inclination toward alternative medical and dietary treatments.[20,21] A meta-analysis of 36 published studies on topical corticosteroids and a six-food elimination diet for EoE showed that the six-food elimination diet resulted in histopathological remission in 69% of individuals and symptom improvement in 87.3% of individuals. Meanwhile, with budesonide treatment, these values were 76.8% and 87.9%, respectively.[22] After any dietary elimination, foods must be reintroduced sequentially with follow-up endoscopy and biopsy to determine the food triggers; symptom-based follow-up alone is inadequate for target food identification.[23]

PPIs

For patients who select a pharmacologic option, EoE is treated with PPIs administered twice daily (BID) for 2 months, and endoscopic/biopsy assessments are repeated before initiating treatment with glucocorticosteroids.[18,20] Extending the treatment period of PPIs to 12 weeks can boost their efficacy by up to 65.2%, compared with a duration of 8–10 weeks.[24] The Appraisal of Guidelines for Research and Evaluation consensus in 2018 stated that the histologic and clinical responses to PPIs ranged from 23% to 83%, with subsequent reports stating substantial variations in PPI dosage and treatment duration as well as a significant level of heterogeneity in the outcomes in pediatric patients.[2,25] The mechanism of action of PPIs for treating EoE is thought to involve reducing eosinophil recruitment to the esophageal epithelium by blocking signal transducer and activator of transcription 6-mediated eotaxin-3 expression.[21,25]

The recent AGA and the JTF EoE guidelines acknowledged unresolved issues related to PPI use in EoE, such as the ideal treatment duration before a repeat endoscopy, optimal PPI dosage, and ideal long-term treatment duration.[25] Any adverse effects of PPIs observed in the treatment of EoE are consistent with those observed in the treatment of other conditions, and this class of medications is considered to be very safe, even with long-term use. Data on the use of PPIs in different conditions have noted possible increases in the risk of *Clostridium difficile* infections, rare (case-reportable) episodes of hypomagnesemia, and some other rare issues; however, recent randomized trial data have alleviated most concerns about prior observational associations that have been reported.[25] As with all treatments, the potential risks and benefits should be balanced for patients opting to use PPIs for EoE.

Esophageal Dilation

Esophageal strictures frequently complicate untreated disease or chronic inflammation in EoE. The AGA/JTF guidelines recommend the use of medical/dietary therapy in conjunction with endoscopic dilation in patients with EoE-associated strictures and dysphagia.[20] Patients with more severe strictures may require dilation before the initiation of anti-inflammatory treatment as well as serial dilatation procedures.[26] Retrospective studies have found that patients with EoE who were effectively treated with medical therapy had lower rates of esophageal dilation.[20,27] Endoscopic dilation is considered an immediate and adjuvant therapy rather than a long-term treatment strategy.[28] It should be noted that dilation primarily addresses the symptoms of dysphagia in EoE and does not treat the underlying inflammation associated with the condition.[16,23] A meta-analysis of 923 articles revealed that dilatation improves dysphagia in 87% of patients but does not decrease the eosinophil count; hence, repeated dilations are necessary to maintain symptom relief when dilatation is employed as the sole treatment for EoE.[23,29] In contrast to early case reports suggesting higher complications during esophageal dilation for treating strictures associated with EoE, extensive studies using a cautious dilation approach revealed that the major complications associated with it were comparable with those encountered during dilation of non-EoE benign esophageal strictures.[20] While chest discomfort is the most common side effect and perforations have been rarely reported, with a more conservative dilation approach, the rate of perforations is only 0.4%, with no mortality. This approach can be advised for all patients with a stricturing EoE phenotype.[29,30]

Corticosteroids

Corticosteroids are considered a mainstay treatment for EoE because they reduce mucosal infiltration of eosinophils, mast cells, T-cells, and cytokines, resulting in the restoration of the epithelial barrier as well as decreased tissue remodeling and fibrosis when prescribed for 6–12 weeks.[18,31] EoE-associated changes in transcriptomes associated with IL-13 can also be significantly reversed by glucocorticoid treatment.[31] This regimen offers additional advantages, including minimal side effects and a favorable safety profile. A randomized controlled trial (RCT) reported that a histological response (reported as peak counts of <15 eos/hpf, <5 eos/hpf, and <1 eos/hpf) was achieved in 60–70% of patients with EoE using budesonide and fluticasone.[32]

In 2018, the EMA approved a budesonide orodispersible tablet (BOT) as the first EoE drug for adults, with a reported 93% efficacy rate for histological remission in 2–6 weeks, with no serious side effects. The BOT also significantly improved symptoms and endoscopic severity compared with placebo.[19] This budesonide formulation has been recently approved by the Saudi Food and Drug Authority (SFDA) as it is easy to use and has demonstrated a favorable safety and efficacy profile in alleviating clinical symptoms and endoscopic abnormalities and enhancing histological response in patients with EoE who do not respond to PPIs.[33,34] However, there have been reports detailing patient intolerance to budesonide, which manifests in the form of bruising, stomach upsets, and throat irritation, due to the presence of sucrose in the formulation. Other side effects include muscle and skin atrophies, striae distensae, or acne.[35,36]

The AGA/JTF recommends topical glucocorticosteroids over oral glucocorticosteroids based on an RCT showing 40% systemic complications with prednisolone vs 15% oral candidiasis with fluticasone.[23] Compared with systemic corticosteroids, adrenal axis suppression is uncommon with topical corticosteroids.[18] A retrospective study observed children under 18 years of age with EoE, with moderate (<9 mm) to severe (<6 mm) strictures, responding clinically and endoscopically to systemic steroids. The children were concomitantly treated with PPIs and diet elimination. Although a small cohort of children was studied, the study suggested that short courses of systemic steroids may be considered as

alternatives to dilation in cases of moderate to severe strictures in children. The short courses of systemic steroids were able to rapidly eliminate the most significant strictures in children, showing that not all strictures are fibrotic but may be inflammatory.[37] This has not been replicated in adults so far. In the 2024 ESPGHAN pediatric EoE guideline update, this treatment remains an option for moderate-to-severe strictures.[38] In a study, 0.5 mg and 1 mg of BOT administered BID for 48 weeks proved effective. It outperformed the placebo in maintaining a remission rate of 75% for adult patients with EoE over 1 year.[39] An optional 96-week open-label extension and a 6-week open-label induction of remission phase, using a recommended dose of either 0.5 mg or up to 1 mg budesonide BID, reported that during this period, more than 80% of patients maintained clinical remission (defined as a weekly EoE Activity Index-Pro score of ≤20) and 81.6% of patients maintained deep histological remission (0 eosinophils/mm^2 in all biopsies) at the end of the 96-week treatment, followed by no loss of efficacy observed over up to 3 years.[39,40] A study identifying CpG methylation sites involved in treatment response to topical corticosteroids showed that reduced methylation within *UNC5B, ITGA6*, and *LRRC8A* was strongly associated with response to topical corticosteroids in patients (n=88) with EoE.[41] The absence of reliable predictors for steroid response remains a significant challenge in the field of EoE. Only a few clinical predictors have been identified. The *TSLP* gene at 5q22 was the first nucleotide polymorphism associated with EoE.[42] Another study analyzed ribonucleic acid sequencing data from prospectively biobanked specimens but found no genes differentially expressed between histologic nonresponders and responders to topical steroids in EoE. However, the study identified a 22-gene module predictive of histological response to topical steroid treatment. Despite this, the module was not validated, and thus, the use of differential correlation to utilize topical steroid treatment based on pretreatment of esophageal biopsies cannot be recommended. Further research using novel techniques and alternative biomarkers is necessary to predict steroid response before initiating treatment for EoE.[43]

Of note, the budesonide oral suspension was approved by the US FDA in 2024 but is not currently available in the Gulf region.[10] The experts reported significant incidences of headache and oral candidiasis with a combination of budesonide and fluticasone. Budesonide seemed relatively inaccessible to patients who did not have insurance coverage.[44] The experts' opinions on the use of budesonide and fluticasone in the management of EoE are as follows:

- PPIs are cost-effective, easily accessible, and commonly favored as a treatment option for EoE.
- Budesonide is easy to use and demonstrates favorable safety, efficacy, and response in patients with EoE who do not respond to PPIs.
- As per the SFDA, budesonide can be considered a step-up therapy until more long-term studies determine its effectiveness.
- Many patients reported intolerance to budesonide in the form of bruising, stomach upsets, and throat irritation due to the presence of a sucrose component in the formulation.
- A combination of budesonide and fluticasone might have side effects such as headache and oral candidiasis. Moreover, instances of patients unable to take budesonide due to lack of insurance coverage were noticed.

Dupilumab

IL-4 and IL-13 and their regulatory pathways have been identified as promising targets treating EoE.[19] Dupilumab, a human monoclonal antibody, targets the α-chain of the IL-4 receptor, which leads to decreased signaling by both IL-4 and IL-13. It is efficacious in treating various type 2 inflammatory diseases such as atopic dermatitis and prurigo nodularis, reducing asthma exacerbations, improving lung function, and reducing polyp size in chronic rhinosinusitis with nasal polyps.[19,45] The efficacy of dupilumab in treating EoE was initially demonstrated in a proof-of-concept clinical trial that showed substantial improvements in dysphagia and histological and endoscopic features compared with a placebo.[46] It demonstrated effectiveness in a Phase 3 clinical trial, which led to its approval by the FDA for EoE treatment in patients aged ≥12 years with a minimum weight of 40 kg.[8] In the dupilumab EoE phase 3 trial, all patients had PPI refractory disease, with 70% of patients having previously tried dietary changes or steroids. A dose of subcutaneous dupilumab 300 mg was administered weekly or fortnightly, and both dosing frequencies demonstrated efficacy in improving eosinophil counts, endoscopic changes, and molecular findings, resulting in histological remission in 60% of the patients. Compared with the placebo, symptomatic benefits were only seen with weekly dosing of dupilumab; this is the basis for the weekly dosing

regimen approved by the FDA.[47] Not only did the EMA approve dupilumab for pediatric use in 2022, but the FDA also approved dupilumab for this age range in 2024, based on data from an additional RCT in children aged 1–12 years. The approvals were granted for different weight-based doses: 200 mg every other week for 15 to <30 kg, 300 mg every other week for 30 to <40 kg, and 300 mg every week for ≥40 kg.[48]

Based on patient characteristics in the adolescent/adult phase 3 trial, dupilumab was helpful as a step-up therapy when other treatments were not tolerated.[49] It may also be beneficial as a step-up therapy in severe or unresponsive EoE cases or as a rescue medication in patients with dilatations, those unresponsive to steroids, those requiring an amino acid-formulated diet, and those with refractory EoE, severe esophageal strictures, or those experiencing adverse effects from their current therapy.[49,50] Literature suggests that in patients with multiple comorbid atopic conditions, such as asthma, atopic dermatitis, and chronic sinusitis with nasal polyps, dupilumab may be useful as a first-line therapy.[49] However, more research and evidence-based recommendations are needed, especially since the use of dupilumab in pediatric populations has been associated with a higher incidence of coronavirus disease 2019, nausea, injection-site pain, and headache compared with that associated with placebo in the same population. The exact positioning of dupilumab in the treatment algorithm for children aged 1–12 years is not yet defined but will likely be similar to that of the older population.

While dupilumab can reduce the need for steroids and dietary restrictions and is shown to be cost-effective for the management of atopic dermatitis, its cost-efficacy is not yet known for EoE.[51] Though total costs incurred with EoE treatment have surpassed $1 billion annually—a substantial sum for a rare condition—and adults with EoE are subjected to more expensive life insurance policies compared with those without EoE, biologics like dupilumab could lead to further elevations in EoE-related costs, mainly due to the weekly dosing regimen for adolescents and adults.[44,49] Therefore, the timing of dupilumab administration must be carefully considered when comparing the usefulness of this medication to those of topical steroids, PPIs, or dietary treatments.[49] Overall, although biologics are considered a primary therapy for EoE, they are more expensive compared with other available treatment options. However, further cost-effectiveness studies are needed for EoE treatment.[49] The experts' opinions on dupilumab and the ideal therapy (treatment algorithm) sequencing for the Greater Gulf region are given below:[52–55]

Expert Opinions on Dupilumab

- The SFDA has recently approved dupilumab for EoE in patients aged >12 years. Previously it was used for patients with severe asthma. The US FDA approved dupilumab for use in patients <12 years of age in 2024.
- Determining optimal dupilumab dosage, particularly in pediatric patients, is challenging due to limited data and recent availability.
- Weekly dosing of dupilumab is not approved for all conditions. There is a lack of current data on patients diagnosed with EoE or the ones with milder EoE symptoms. In such cases, a lower dosage schedule should be considered.
- Dupilumab has demonstrated clinical efficacy in treating patients with advanced EoE stages and fibrosis. However, additional evidence is required to support the findings.
- The current data on dupilumab use in pregnant women or in women trying to conceive are limited.

Expert Opinions on the Ideal Therapy (Treatment Algorithm) Sequencing for the Greater Gulf Region

- Clinical applications of the Index of Severity (I-SEE) aid in treatment decisions and patient outcomes in EoE.
- Further research on gene expression and epigenetic changes can help predict corticosteroid treatment responses.
- Steroid therapy or dietary elimination may be considered a first-line treatment for patients with a confirmed EoE diagnosis and food impaction.
- The experts suggest utilizing EoE-specific treatment, such as BOT or dupilumab, in pediatric cases.
- The experts deliberated whether early interventions with approved biologics can help manage EoE and control disease progression, although additional data are required for this.
- For patients with esophageal fibrosis unresponsive to persistent or multiple dilations, dupilumab may be considered as a potential first-line treatment, considering factors such as patient preference, logistics, and cost compared with corticosteroids.
- Although dupilumab shows promising results compared with steroids and PPIs, drug accessibility and insurance coverage for weekly dosing remain a problem.

- Dupilumab needs a dose-tapering strategy to prevent potential flare-ups.

The experts stated that the clinical application of I-SEE for EoE will aid in treatment decisions and patient outcomes. The advantages and disadvantages of the different drugs are provided in Table 1.[23,25,31,40,46,49,50,55–57]

Knowledge Gaps and Pathways Forward

Diagnostic Dilemma

Even in cases meeting the diagnostic criteria for EoE, it can be challenging to distinguish EoE from gastroesophageal reflux disease (GERD), and it is necessary to determine if there is overlapping GERD and whether it contributes to symptomatology.[4,58] Another dilemma is the lack of consistency between symptoms and histology in EoE. In particular, it is important to assess whether there are persistent symptoms despite endoscopic and histologic remission, other concurrent conditions (such as GERD or atopy), esophageal dysmotility, and esophageal hypersensitivity or hypervigilance.[18] If persistent symptoms are dysphagia-predominant, it is essential to assess for any subtle stricture or narrowing, as these can be missed during routine endoscopy.[59]

A set of validated tools for diagnosing EoE may help improve the correlation between inflammation and observed symptoms in patients with EoE.[58] Recent advances such as clinician-reported outcomes, Eosinophilic Esophagitis Activity Index, Dysphagia Symptom Questionnaire, and the endoluminal functional lumen imaging probe should be further investigated to assess their accuracy in predicting the biological activity of EoE.[58]

The diagnosis of EoE depends on a combination of esophageal symptoms, endoscopic observations, and eosinophils in histological samples.[18] Currently, recommendations for the diagnosis of EoE include ensuring adequate esophageal sampling, which involves obtaining a minimum of six biopsies.[58] Unfortunately, noninvasive testing or blood-based biomarkers are not yet routinely used or validated for clinical care.[58] Therefore, this remains an important area of future research for diagnosing and monitoring EoE.

Treatment Choices

Clinically applicable treatment algorithms can be developed to assist practitioners in making informed decisions regarding patient care. Specifically, the ambiguity regarding positioning various therapeutic approaches (diet, drugs, PPIs, swallowed topical steroids, biologic agents, and novel small molecules under development) in an algorithm must be addressed. However, the lack of comparative efficacy studies makes this problematic.[50] Recent AGA/JTF guidelines align with collaborative,

Table 1 Advantages and Disadvantages of the Drugs Used for Managing EoE[23,25,31,40,46,49,50,55–57]

Drug	Advantages	Disadvantages
PPIs	• Cost-effective • Easily accessible • Commonly favored as an initial treatment option for EoE	• Suboptimal efficacy • Off-label
Budesonide	• SFDA-approved • More efficacious than PPIs • Efficacious in patients with EoE who are unresponsive to PPI therapy • Well tolerated	• Rare adrenal side effects and intolerance • Loss of long-term response
Dupilumab	• SFDA has approved the use of dupilumab in KSA and UAE for patients aged >12 years • Proven efficacy in reducing symptoms, improving histology, and addressing endoscopic findings in patients with EoE, particularly those who have failed PPIs and have tried other treatments • Dupilumab could be considered a first-line treatment for severe EoE cases, especially for patients with a narrow caliber phenotype who require multiple dilations	• High cost • Requirement for weekly self-administered injections • Long-term safety and efficacy are yet to be determined • Lack of data on newly diagnosed or treatment-naïve patients • The use of dupilumab is associated with several ocular side effects ranging from mild to severe manifestations[57]

Abbreviations: EoE, Eosinophilic esophagitis; KSA, Kingdom of Saudi Arabia; PPI, Proton pump inhibitor; SFDA, Saudi Food and Drug Authority; UAE, United Arab Emirates.

shared decision-making in the absence of definitive therapy for EoE, as each therapeutic approach presents its own set of trade-offs.[50] The EMA has newly authorized dupilumab for treating EoE in adults and adolescents over 12 years of age. The inclusion criteria for dupilumab use in such cases are patients who weigh at least 40 kg, are inadequately controlled by, or are intolerant to conventional treatments.[60] A recently updated algorithm for EoE treatment recommends using the anti-IL-4/13 antibody dupilumab for patients resistant to conventional treatment.[61] The criteria and rationale for maintenance therapy in patients with EoE remission should be addressed further. A recent consensus advocated dose tapering of PPIs to maintain disease remission until a long-term therapeutic approach was clearly defined.[58] Performing endoscopy after initiating treatment or making changes to the treatment was also endorsed by a multidisciplinary group from both the US and Europe.[56] Emerging minimally invasive technologies, such as cytosponge and esophageal strings, have high sensitivity and should be evaluated for treatment monitoring plans.[62] A recent study has postulated a therapeutic pyramid model to introduce a hierarchical perspective for treating EoE. However, PPIs, corticosteroids, antibody treatment, and diet elimination remain the prime approaches. The pyramid suggested a tiered approach for EoE treatment dependent on the mechanistic profile, the disease phenotype, the efficiency and safety of the drugs used, cost-effectiveness, and QoL.[63] New biological therapies and other compounds are being researched and may soon alter the current treatment protocols.[64]

The diagnosis of EoE is evolving as new technologies are being explored. While current monitoring practices include patient-reported outcomes, fluoroscopy, and endoscopy, some sites are using new technologies such as functional luminal imaging probes and transnasal endoscopy (TNE). Noninvasive biomarkers, such as the string test and cytosponge, are being investigated. The monitoring standards for EoE will continue to develop, thereby benefiting both patients and providers by offering better insight into disease progression.[42] A better understanding of disease genotype and transcriptome can enable more personalized diagnostics and therapeutics, making the future of personalized medicine for EoE promising.[42]

Addressing the knowledge gaps pertaining to EoE in the Greater Gulf region is essential for improving patient outcomes. There is a dearth of literature on epidemiological data for EoE in this region. Therefore, multicenter regional studies should be initiated to assess the prevalence, incidence, and clinical characteristics of patients with EoE. These studies could offer a better understanding of the disease burden in the region. Moreover, establishing Gulf-specific diagnostic criteria and treatment guidelines could ensure effective management of EoE. Multidisciplinary collaboration through workshops and conferences involving specialists from different Gulf countries can help improve treatment protocols and ensure uniform practices across the Gulf region.

Limitations

This study, which is based on expert opinions from specialists across the Greater Gulf region, has specific limitations. The study outcome is based on the answers to questions put forward by experts; hence, the results may be highly subjective. The expert opinions are based on individual experiences and may lead to potential biases in the generalization of the statements. Comprehensive clinical representation cannot be based solely on the study outcome.

Conclusion

Over the last 20 years, EoE has emerged as a major cause of dysphagia and a significant contributor to upper gastrointestinal disease morbidity. However, robust evidence and data have provided insights into effective management strategies for EoE. Dietary elimination, PPIs, and topical steroids are typically considered the first-line treatment options. Given the increasing demand for less invasive techniques, TNE can be considered over the traditional sedated esophagogastroduodenoscopy (EGD) when evaluating pediatric EoE. Unlike traditional EGD, TNE offers several advantages, such as being able to be performed in an outpatient clinic, not requiring anesthesia or sedation, utilizing a small endoscope that is tolerated by adults, and providing sufficient samples for evaluating Barrett's esophagus. Thus, TNE is a cost-effective and novel procedure offering new possibilities for monitoring EoE in both children and adults. This expert opinion has summarized the newly published global recommendations for biologics and novel therapies, discussed treatment strategies and existing knowledge gaps, and identified areas for future research. Addressing the educational gaps within the Greater Gulf region could significantly improve patient outcomes by ensuring that healthcare professionals are equipped with the latest knowledge and best practices in diagnosis and treatment. Even high-income economies, such as the Gulf region, still face several challenges in managing EoE. Therefore, addressing the challenges

and knowledge gaps pertaining to EoE in the Greater Gulf region has the potential to influence EoE management practices globally. The insights gained from the Gulf region could refine global diagnostic and treatment strategies for EoE, ultimately leading to better outcomes for patients with EoE worldwide.

Abbreviations

AGA, American Gastroenterological Association; BID, Twice daily; BOT, Budesonide orodispersible tablet; EGD, Esophagogastroduodenoscopy; EMA, European Medicines Agency; EoE, Eosinophilic esophagitis; FDA, Food and Drug Administration; GERD, Gastroesophageal reflux disease; HPF, High-power field; IgE, Immunoglobulin E; IL, Interleukin; I-SEE, Index of Severity; JTF, Joint Task Force; PPI, Proton pump inhibitor; QoL, Quality of life; RCT, Randomized controlled trial; SFDA, Saudi Food and Drug Authority; TNE, Transnasal endoscopy; US, United States.

Data Sharing Statement

All the data in this study are from published sources.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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