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Position Paper

Eosinophilic esophagitis: Update in diagnosis and management. Position paper by the Italian Society of Gastroenterology and Gastrointestinal Endoscopy (SIGE)

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ABSTRACT

Eosinophilic esophagitis (EoE) is a chronic immune-mediated disease of the esophagus characterized by symptoms related to esophageal dysfunction, as well as significant esophageal eosinophilia.

The entity exists worldwide but has been most extensively studied in Western countries. However, a wide range of symptoms has been noticed such as chest pain or gastro-esophageal reflux disease-like symptoms. Upper gastro-intestinal endoscopy and esophageal biopsies are crucial for the diagnosis. Endoscopy might be normal or reveal typical patterns such as rings, furrows, exudates, edema, and stricture. Two to four biopsies should be performed both in the distal and in the proximal esophagus, and 15 eosinophils per high power field within the esophageal epithelium are the minimal threshold to diagnose eosinophilic esophagitis.

Allergy testing is recommended, although its impact to orient treatment remains to be demonstrated. Eosinophilic esophagitis treatment includes medical treatment, diet and endoscopic dilation. Proton pump inhibitors are the first-line therapy as up to 50% of patients respond well to proton pump inhibitors irrespective of objective evidence of GERD. Topical viscous corticosteroids or elimination diet are the treatment of choice in case of unresponsiveness to proton pump inhibitors.

1. Introduction

Eosinophilic esophagitis (EoE) is a chronic immune-mediated disease of the esophagus characterized by symptoms related to esophageal dysfunction, as well as significant esophageal eosinophilia [1].

EoE represents an up and coming disease entity with some proven evidences and many open questions that need to be resolved.

These guidelines, which mainly address EoE in adults, reflect the position of the Italian Society of Gastroenterology (SIGE) on this topic; they put forward recommendations regarding fundamental clinical questions pertaining to the management of EoE. These recommendations are summarized and highlighted in Table 1.

In order to assess the strength of our recommendations and the evidence, the GRADE system was used [2]. Recommendations were either strong (desirable effects outweigh undesirable effects) or conditional (trade-offs are less certain), and the quality of evidence was either strong (further research is unlikely to change confidence in the estimate), moderate (further research is likely to change confidence in the estimate), low (further research is very likely to change confidence in the estimate), or very low (the estimate of the effect is very uncertain) [2]. Current management of adult EoE is depicted in Fig. 1.

Statement 1. EoE is currently defined as a chronic, immune-mediated esophageal disease characterized by symptoms related to esophageal dysfunction and eosinophil-predominant inflammation [3].

(Recommendation: strong; Evidence: moderate)

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Table 1
Highlights in management of adult EoE.

Definition and diagnosis
Definition of eosinophilic esophagitis (EoE) and diagnostic criteria 1. EoE is a clinico-pathological disease diagnosed by taking into account symptoms, endoscopy and histopathological findings. Currently, EoE is defined by the following criteria: • Symptoms related to esophageal dysfunction. • Peak concentration ≥15 eosinophils/high-power field (EOS/HPF). • The eosinophilic infiltrate is confined to the esophagus. • Exclusion of other disorders associated with esophageal hypereosinofilia.
2. Esophageal biopsies are essential for EoE diagnosis. A minimum of 2–4 biopsies at the level of the proximal and distal esophagus are recommended.
3. Proton pump inhibitor-responsive esophageal eosinophilia (PPI-REE) is no longer considered an exclusion criterium for EoE, but as belonging to the clinical spectrum of EoE.
4. Response to PPIs has no correlation with gastroesophageal reflux disease.
Treatments Therapeutic endpoints in EoE 5. EoE therapy aims to improve clinical symptoms and eosinophilic infiltration in the esophagus, in order to obtain a complete regression of the disease.
6. Symptoms are an important marker of therapeutic response in EoE but need to be coupled with results of endoscopy and biopsies in order to properly evaluate disease activity and response to therapy.
7. The first line treatment of EoE is generally represented by PPIs for at least 8 weeks.
8. Topical steroids (i.e. budesonide for an initial period of 8 weeks) are generally prescribed after failure of PPI therapy.
9. Patients without symptomatic and histological improvement after topical steroids may benefit from treatment with a higher dose, or with systemic steroids, or with dietary elimination.
10. Dietary elimination may also be considered as an initial therapy of EoE.
11. The decision to use a specific dietary approach (elemental, empiric, or targeted elimination diet) should be tailored to individual patient needs and available resources.
12. Endoscopic esophageal dilation is an effective therapy in symptomatic patients with strictures that persist in spite of medical or dietary therapy.
13. Long term treatment with half dose of the effective drug is presently recommended.

Legend: EoE: eosinophilic esophagitis; EOS: eosinophils; HPF: high power filed; PPI-REE: proton pump inhibitor-responsive esophageal eosinophilia; PPI: proton pump inhibitors.

1.1. Summary of evidences

Eosinophilic infiltration of the esophagus was first described in the 1990s, and later it was recognized to be independent from condition from the presence of gastroesophageal reflux disease (GERD) [4].

The main characteristic of EoE is that it is a disorder triggered by food and/or aeroallergens. Although the etiology remains unknown, the predisposition or the presence of documented allergic condition remains the most likely possibility. In fact, several studies have suggested a central role of food allergies and aeroallergens as possible etiologic agents [3,5–7]. EoE is defined by the presence of ≥15 eosinophils in at least one high-power field (HPF) found in one or more of the esophageal mucosa biopsies [1]. Evidences on histopathology are debated below.

Statement 2. Proton pump inhibitor-responsive esophageal eosinophilia (PPI-REE) should be diagnosed when patients have esophageal symptoms and histological findings of EoE, but achieve clinical and histological remission on PPI therapy. The latest guidelines suggest that PPI-REE represents a clinical entity belonging to the clinical spectrum of EoE and this term should no longer be used [8].

(Recommendation: strong; Evidence: moderate)

1.2. Summary of evidences

Proton pump inhibitor-responsive eosinophilic esophagitis (PPI-REE) comprises a distinct subgroup of patients, around 50% of all patients, presenting clinical and histological findings of EoE but, at the same time, a clinical response and a complete regression of the eosinophilic infiltrate of the esophagus following a PPI therapy, in the absence of clinical or pathophysiological features of GERD [9,10].

Furthermore, recent studies have shown that esophageal mediators of eosinophlic inflammation, such as eotaxin-3 (a chemoattractant that plays a major role in the pathogenesis of EoE), have similar levels and esophageal transcriptome is within the same molecular spectrum in PPI-REE and EoE, but much different in GERD [11,12]. Thus in 2016 an international task force proposed that PPIs not be used a as a diagnostic tool, but rather as first line treatment, before diet and steroids [8].

In the present paper PPI-REE will be considered as a clinical entity belonging to EoE and the term PPI-REE will not be mentioned any longer.

Statement 3. EoE is a condition with an apparent increase of incidence.

(Recommendation: strong; Evidence: moderate)

1.3. Summary of evidences

Currently, EoE occurs in children and adults, males and females, and in individuals from a range of ethnic backgrounds with equal probability [1]. The highest prevalence of EoE has been reported from North America, Sweden [13,14], and Australia [15], with an incidence estimated around 5–7/100.000 inhabitants and a prevalence estimated around 50–60/100.000 inhabitants. In Europe, the main data come from Switzerland with an estimated prevalence of about 23/100.000 inhabitants [16].

A recent population-based Canadian study found that an increase in the EoE incidence from 2,1 per 100.000 to 11,0 per 100.000 persons was significantly influenced by a higher rate of obtaining esophageal biopsies [17], even if, at the same time, the