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REVIEW IN GASTROENTEROLOGY

Eosinophilic oesophagitis: Current evidence-based diagnosis and treatment☆

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Abstract Eosinophilic oesophagitis (EoE) is a disease caused by an immune response to food antigens in contact with the oesophageal mucosa. Its diagnosis is defined by the combination of oesophageal dysfunction symptoms and inflammation of the oesophageal mucosa predominantly by eosinophils. Its chronic course and frequent progression to subepithelial fibrosis and oesophageal strictures indicate the need for treatment. The information provided by recent clinical trials and systematic reviews has led to the development of new clinical guidelines, endorsed by several European scientific societies. This review includes the most relevant aspects of the new guidelines, updates the EoE concept and reports its epidemiology and risk factors, associated conditions and its natural history in children and adults. Diagnostic criteria are provided, and tests for EoE diagnosis and monitoring and therapeutic options are analysed based on the best scientific evidence and consensus opinion of experts.

PALABRAS CLAVE
Esofagitis eosinofílica;
Diagnóstico;
Tratamiento;
Práctica clínica basada en la evidencia

Esofagitis eosinofílica: diagnóstico y tratamiento actual basado en la evidencia

Resumen La esofagitis eosinofílica (EoE) es una enfermedad causada por una respuesta inmune frente a antígenos alimentarios en contacto con la mucosa esofágica. Su diagnóstico se define por la combinación de síntomas de disfunción esofágica e inflamación de la mucosa esofágica, predominantemente eosinofílica. Su curso crónico y la frecuente progresión hacia fibrosis subepitelial y estenosis esofágicas indican la necesidad de tratamiento. La información proporcionada por ensayos clínicos y revisiones sistemáticas recientes ha permitido desarrollar

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una nueva guía clínica, avalada por varias sociedades científicas europeas. Esta revisión recoge los aspectos más relevantes de la nueva guía, actualiza el concepto de EoE, informa de su epidemiología y factores de riesgo, condiciones asociadas y su historia natural en niños y adultos. Se proporcionan los criterios diagnósticos, se analizan las pruebas para diagnóstico y monitorización de la EoE, y las opciones terapéuticas en base a la mejor evidencia científica y la opinión consensuada de expertos.

Introduction

Eosinophilic oesophagitis (EoO) is a chronic inflammatory disease of the oesophagus. It is characterised clinically by symptoms related to oesophageal dysfunction and histologically by eosinophil-predominant inflammation of the oesophagus. Since the initial characterisation of EoO as a separate clinical pathological syndrome from eosinophilic gastroenteritis in the early 1990s by two independent groups of researchers,[1,2] its prevalence has increased dramatically, affecting at least one in every 2000 inhabitants in Europe and North America.[3] As a result, EoO is currently the second most common cause of chronic oesophagitis after gastro-oesophageal reflux disease (GORD) and the main cause of dysphagia and food impaction in children and young adults. Although it is not associated with mortality or risks of malignancy, its chronic nature and progressive behaviour adversely impact patients' quality of life.[4]

Over the two decades of the disease's history, the volume of scientific evidence available on the different epidemiological, pathophysiological, clinical and therapeutic aspects of EoO has grown exponentially and has been summarised in four consensus documents and clinical practice guidelines developed by expert groups.[5–8] However, major advances over recent years, including several randomised, placebo-controlled clinical trials (RCTs) and meta-analyses with systematic reviews, which are not included in earlier guidelines, mean that these are currently obsolete. Furthermore, the overall quality of all earlier guidelines (evaluated using the AGREEII tool) is limited since no specific methods were used to establish the quality of evidence or the weight of the statements and recommendations they provided.[9]

New clinical guidelines developed by an international group of experts using the GRADE system to classify evidence and the strength of recommendations have just been published under the auspices of *United European Gastroenterology*.[10] The recommendations were based on the best available evidence, and when such evidence was not available or was considered to be inconsistent, consensus was sought among expert authors and the best clinical practice. After two rounds of voting, the recommendations were decided upon by consensus at a final face-to-face meeting. The new guidelines[10] (the main recommendations are presented in this review) aim to provide doctors who treat children and adults with EoO (including gastroenterologists, allergists, paediatricians, ear, nose and throat specialists, pathologists, dieticians, general practitioners and emergency doctors) with a structured framework for the diagnosis and treatment of the disease.

Definition of eosinophilic oesophagitis: evolution and current concept

According to the latest definition, EoO is a chronic, immune-mediated oesophageal disease characterised clinically by symptoms related to oesophageal dysfunction and histologically by eosinophil-predominant inflammation. Clinical manifestations and histological findings should not be interpreted in isolation, and other local and systemic causes of oesophageal eosinophilia should be excluded (Table 1).

The first guidelines for EoO, published in 2007, considered the presence of symptoms of oesophageal dysfunction, eosinophilic infiltration of the oesophagus (defined by epithelial biopsies with >15 eosinophils per high-power field), together with lack of response to proton pump inhibitors (PPI) or, alternatively, normal oesophageal acid exposure determined by pH-metry, as diagnostic criteria.[5] A dichotomous diagnostic criterion was established that assumed that GORD and EoO were mutually exclusive disorders, with GORD being the only oesophageal disease capable of responding to PPI therapy. However, this assumption was counterintuitive since the likelihood of both diseases coexisting in the same patient was high, usually affecting young males.[11] In 2011, the first prospective series to systematically evaluate PPI therapy in patients with oesophageal eosinophilia and symptoms suggestive of EoO showed that up to 50% responded to PPIs.[12] Furthermore, there was no significant difference in clinical, endoscopic and histological findings between PPI responders and non-responders and as a result, there was an extensive overlap between GORD (determined by monitoring oesophageal pH) and EoO. After this study, subsequent guidelines excluded oesophageal pH monitoring as a criterion for EoO diagnosis,[6] but continued to consider response to PPI as sufficient motive to rule out EoO. The definition of a novel potential phenotype of the disease in 2011, called ''PPI-responsive oesophageal eosinophilia'', to classify patients with features of EoO who achieved complete remission with PPI therapy, replaced GORD as the main differential diagnosis of EoO. Since 2011, numerous studies have clearly demonstrated that PPI-responsive patients not only share clinical, endoscopic and histological features but also molecular features.[11] No other inflammatory gastrointestinal disease, except for ''PPI-responsive oesophageal