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Medical therapy in eosinophilic oesophagitis



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A B S T R A C T

Eosinophilic oesophagitis (EoE) is a chronic-inflammatory disease of the oesophagus. If left untreated, eosinophilic inflammation induces fibrosis, angiogenesis and stricture formation, resulting finally in a so called remodelling with structural and functional damage of the organ. In addition, patients with untreated EoE are permanently at risk of experiencing food impactions. It is therefore widely accepted that active EoE should be treated. Any treatment applied in EoE should ideally achieve two therapeutic goals: first, resolution of symptoms, and, second, control of inflammation. Avoidance of food allergens by elimination diets as well as anti-inflammatory drugs have both the ability to achieve these goals. Among the pharmacological options, only corticosteroids have documented efficacy, whereas alternatives have shown rather disappointing results or are still under evaluation. Of note, swallowed topical corticosteroids are at least as efficient as systemically administered corticosteroids but have fewer side effects. As such topical corticosteroids are widely used as first-line drug in the treatment of EoE, even though this compound is currently not approved for this indication by regulatory authorities. Unfortunately, complete resolution of symptoms can be achieved with swallowed topical corticosteroids only in approximately 70% of patients despite appropriate dosing and despite correct administration of these compounds. Control of inflammation is even harder to achieve, as only in approximately 50% of patients tissue eosinophilia disappears completely under this anti-inflammatory medication. For this group of “difficult to treat” patients, therapeutic alternatives are urgently needed. Fortunately several anti-allergic drugs and several biologicals are currently under investigation.

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Introduction

Eosinophilic oesophagitis (EoE), a distinct clinico-pathologically defined syndrome, was first recognized and described in the early 1990s [1,2]. Dysphagia and food impaction are the typical manifestations in adults, whereas in children, food refusal and failure to thrive are the predominant symptoms [3–5]. Prior to those first papers describing EoE as its own distinct entity, single case reports attributed oesophageal eosinophilia to a variety of already described disorders, such as gastro-oesophageal reflux, achalasia or eosinophilic gastroenteritis [5]. EoE was originally regarded as something of a curiosity. However, due to increasing incidence of EoE in westernized countries [6,7], it has now reached a prevalence comparable to that of Crohn's disease and is likely to be the most common cause of both dysphagia resulting from ingestion of solid food and spontaneous perforation of the oesophagus [6]. Two decades of intense research has uncovered many molecular, immunological and clinical aspects of this chronic-inflammatory disorder. In addition, EoE experts have been instrumental in establishing diagnostic and therapeutic recommendations [4].

In this article, we will focus exclusively on the pharmacologic treatment of EoE, in particular on indications for treatment, therapeutic goals, the currently available options and the practical performance of pharmacotherapy.

Indications for treatment of eosinophilic oesophagitis

When scientific community is confronted with a new disease, the understanding of its natural course is crucial before any treatment modality can be considered. The first natural history study has demonstrated that EoE is a chronic disease, and that symptoms as well as inflammation persist over the years [8]. As such, the quality of life of EoE patients is substantially impaired as long as EoE is not properly treated [3–5]. Improvement of quality of life is therefore a first indication for treatment.

In addition, basic science research and clinical studies have accordingly confirmed that an ongoing active eosinophilic oesophageal inflammation leads to deposition of subepithelial fibrous tissue in the oesophageal wall [9–11]. This so-called “remodelling” induces alterations that finally result in a rigid and fragile oesophagus with impaired function [3–5]. It is well documented, that this process can be prevented or even reversed by an efficient anti-eosinophil treatment [11,12]. Organ preservation can therefore be regarded as a second, important indication for treatment.

Finally, EoE patients frequently experience long-lasting food-impactions requiring endoscopic interventions [13]. This complication harbours a risk for oesophageal injury, either caused by retching or by improperly performed endoscopic intervention. Food impactions are mostly observed in non-adequately treated patients. A recently published retrospective study has confirmed this observation and shown that patients treated with an anti-eosinophil medication experience significantly less long-lasting food impactions when compared to non-treated patients [14]. Prevention of this unforeseeable EoE complication is therefore a further indication for treatment.

In summary, clinically and histologically active EoE should be treated with anti-eosinophil medication because this measure has potential: first, to diminish symptoms and to improve therefore the quality of life of EoE patients; second, to prevent oesophageal damage caused by tissue remodelling due to unbridled eosinophilic inflammation; and third, to reduce the risk of severe oesophageal injury by preventing long-lasting food impactions.

Treatment goals in eosinophilic oesophagitis

At present, the target of EoE treatment is still a subject of intensive debate. Should the treatment result in the improvement of symptoms or in the normalisation of altered biologic measures or even in both? In the absence of agreement on meaningful therapeutic endpoints, a uniform treatment algorithm for EoE patients is still lacking [4,5]. In general, as stronger the relationship between an altered biological marker and organ damage is, the more critical it is to include it in the therapeutic concept [15]. It is evident that resolution of symptoms is the first goal of EoE treatment. However, given the fact the ongoing eosinophilic inflammation in EoE results in a long-term organ damage – as is the case in

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