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Research Article

# Effect of Ingested Fluticasone Propionate on Eosinophilic Oesophagitis

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## Abstract

Eosinophilic oesophagitis (EoE) is characterized by upper gastrointestinal symptoms and of more than 15 or 20 eosinophils in the esophageal epithelium. Lack of awareness to EoE among some gastroenterologists made the disease under recognized. Patients with eosinophilia oesophagitis should be referred to both an allergist and gastroenterologist for optimal management, which may include dietary modifications, pharmacologic agents, ingested fluticasone and its role in EoE will be discussed in this study. This study was conducted at faculty of medicine, Alexandria University, internal medicine, tropical medicine department, and gastroenterology and endoscopy unit. The study was conducted on twenty patients who were complaining from recurrent dysphagia and done upper GIT endoscopy and diagnosed histopathologically as E0E. The 20 patients were randomly assigned to receive either placebo (n = 10) or swallowed fluticasone (n = 10). Patients received two puffs four times a day, with 200 micrograms per puff. Treatment lasted four weeks and follow up extended up to 8 months. The fluticasone was delivered via a metered-dose inhaler without the spacer. After 4 weeks treatment, Clinical symptoms and histological changes were evaluated. Histologic improvement in the form of full histological remission was seen in seven patients in the fluticasone group compared with one patient who achieved remission in the placebo group. In conclusion, the study highlights the problems of diagnosis and lack of awareness and understanding of the etiology and pathogenesis of the disease. The use of ingested fluticasone showed improvement of symptoms, and histological pattern.

***Keywords:*** *Oesophagitis; Eosinophilic; Fluticasone; Endoscopy; Pathology*

## Introduction

Eosinophilic Oeosophagitis (EoE) is a chronic, immune / antigen mediated, esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil predominant inflammation. Eosinophilic oesophagitis is a rarely diagnosed condition involving eosinophil infiltration of the oesophageal mucosa and creating significant dysphagia. Failure to diagnose this disorder relates to reluctance to biopsy an apparently normal oesophagus. This is essential for histological diagnosis [1]. Endoscopy and biopsies are considered the only reliable EoE diagnostic tests. Endoscopic features (trachelization, longitudinal furrows) can suggest but cannot diagnose EoE [2].

Gastric, duodenal or other infiltrate areas biopsies should be examined to exclude other potential causes of eosinophilic inflammation. By definition, EoE is isolated to the eosophagus.15eosinophils/hpf (peak value) is considered a minimum threshold to make a diagnosis of EoE. Gastroesophageal reflux disease (GERD) should be excluded before making the diagnosis of EoE [3]. Dysphagia, Odynophagia, food Impaction, GERD unresponsive to medical or surgical therapy, abdominal Pain, vomiting, anorexia and early satiety may be the GI complain [4].

Most recent literature refers to EO but may escape diagnosis due to lack of awareness of this as a separate pathology. Beside food sensitivity, sensitivity pollen allergens are also common in EoE [5]. Isolated case reports have documented a correlation between pollen allergy skin test results and seasonal changes in EoE symptoms and esophageal eosinophil levels [6].

EoE is a combined disorder involving IgE non-IgE-mediated immune mechanisms. As a result, methods to diagnose IgE-mediated allergy are useful to detect culprit foods, but will not detect those causing symptoms through a non-IgE mediated mechanism. The most common foods identified by Spergel., *et al*. were milk, wheat, corn, beef, egg [7].

Endoscopy with Biopsy is the only reliable EoE diagnostic test. Many endoscopic features associated with EoE were reported like loss of vascular pattern and longitudinal furrowing of the esophagus. White exudates are the gross manifestation of eosinophilic pus and correlate with the histological finding of eosinophilic abscesses. Concentric rings may be transient, indicating esophageal contraction, or fixed, indicating tissue remodeling with stricture formation. When esophageal pinch biopsies are obtained, the mucosa may feel rubbery at inflamed sites owing to fibrosis, thus making tissue samples more difficult to obtain compared with no inflamed sites. Long-caliber esophageal narrowing or small-caliber esophagus and perforation are unusual but also has been reported [8-10].

Management of these patients has been made difficult due to diagnostic problems and a poor understanding of the disease pathogenesis. Antihistamic medications have been used but with no reported success.

Oesophageal dilatation has been tried for symptomatic relief but unfortunately this provides only short term relief [11].

Some medications are currently approved to treat EoE. Corticosteroids are the most helpful medications for treating EoE. At first, higher doses may be needed but they are associated with a many side effects [12]. Dietary therapy-Amino acid based formulas and dietary elimination are very effective therapies for children with EoE; However, its use in adults requires further study. Consultation with dietitian is necessary to insure adequacy of calories, protein and micronutrients with removal of allergic foods [13]. Topical corticosteroids are effective therapy for EoE in children and adults. Systemic corticosteroids are used for emergent situations but not for chronic management of EoE [14].

Endoscopic food disimpaction and esophageal dilation may be necessary in some patients with eosinophilic oesophagitis, dilation provides relief of dysphagia. In some patients, a trial of medical or dietary therapy dilation may be used. Other treatments-Cromolyn sodium, leukotriene receptor antagonists, and immune-suppressive drugs (azathioprine or 6-MP) have shown some benefits in the treatment of EoE [15]. Topical steroid therapy can be used as a treatment. Fluticasone propionate and betamethasone can be sprayed into the mouth without a spacer and dry-swallowed to provide topical anti-inflammatory effect to the oesophageal body very small amounts are absorbed and systemic side effects are therefore minimal [14].

Fluticasone propionate has potent anti-inflammatory actions. When used as an inhaler, fluticasone propionate reduces inflammation in the airways of patients with asthma, thus relieving wheezes and breathing difficulties. When fluticasone propionate is swallowed, it has been shown to reduce the eosinophils in the esophagus and relieve dysphagia in patients with eosinophilic oesophagitis [16]. Fluticasone comes in two types of delivery devices:

- Metered dose inhalers (MDI)
- Diskus

The MDI should be used to treat EE since the diskus is designed to increase steroid delivery to the lungs mainly [17].

In treating eosinophilic oesophagitis, Patients are told not to eat or drink for two hours after each dose. Improvement in dysphagia usually is within weeks. Most patients relapse after stopping treatment [16].

When used in low doses, therefore side effects are minimal. One of the side effect is thrush stomatitis, which is easy to treat. Side effects of high doses of fluticasone propionate are similar to that of oral steroids [18].

### Aim of the work

The aim of this study was to detect the effect of ingested Fluticasone Propionate on Eosinophilic Oesophagitis.

### Patients and methods

This study was conducted at faculty of medicine, Alexandria University, internal and tropical medicine department, Gastroenterology and endoscopy unit. The study was conducted on twenty patients diagnosed histopathologically as EoE (upper Endoscopy with Multiple (2 - 4) biopsies each from the proximal and distal esophagus were obtained and histopathologically examined). The 20 patients were randomly assigned to receive either placebo (n = 10) or swallowed fluticasone (n = 10). Patients received two puffs four times a day, with 200 micrograms per puff for four weeks. The fluticasone was delivered via a metered-dose inhaler without the spacer (to swallow the medication rather than inhale it). After 4 weeks treatment, Clinical symptoms and histological changes were evaluated.

EoE is characterized histologically by dense epithelial eosinophilia , The limited size of endoscopic mucosal biopsies (3 mm in diameter or less) prevent characterization as to the depth of this inflammation, Diagnosis of eosinophilia is focused primarily on the peak number of eosinophils per high-power field (HPF) present in the epithelial surface; the most sensitive and specific threshold number of eosinophils (peak or mean) in the mucosal biopsy that correctly identifies patients with EoE is ≥ 15 eosinophils per single HPF was chosen as the threshold number for the diagnosis of EoE [19]. Epithelial surfaces affected by EoE may also demonstrate features such as superficial layering of eosinophils and micro-abscesses on the superficial layer, these findings are the histological representations of the endoscopic feature termed white exudates or eosinophilic pus. Other commonly identified histological features observed in some biopsies include basal zone hyperplasia, rete peg elongation, intracellular edema, and dilated intercellular spaces [20].

## Results

Among our patients, there was 8 patients with no endoscopy findings. However, 4 patients (20%) showed loss of vascular pattern and longitudinal furrowing of the oesophagus. Moreover, white exudate was detected in 8 patients (40%) (Table 1).

| Endoscopic Findings | Patients (No = 20) |
|---|---|
| Normal Endoscopy | 10 (50%) |
| Loss of vascular pattern and longitudinal furrowing of the oesphagus | 4 (20%) |
| White exudate | 6 (30%) |

***Table 1:*** *Endoscopic findings among the patients groups.*

After receiving the drug for one month and follow up of both groups for about 8 months by clinical symptoms evaluation and re-endoscopy. Histologic improvement was seen in seven patients (Table 2) in the fluticasone group compared with one patient (10%) in the placebo group. None experienced systemic adverse effects of corticosteroids in the fluticasone group. 2 patients (20%) of patients in fluticasone group experienced candida esophagitis compared none in the placebo group. Starting from week 20 to 24 after stopping treatment 3 patients (30%) of those were receiving fluticasone showed the symptoms of eosinophilic oesophagitis. By week 32, about 50% of patients in fluticasone group had symptoms recurrence (Figure 1 and 2). However, there was no clinical improvement in 9 patients (90%) of the placebo control group.

| Histological Improvement | Gp I: on Fluticasone (No =10) | Gp II: on Placebo (No =10) | Chi Square |
|---|---|---|---|
| Improvement | 7 (70%) | 1 (10%) | P = 0.001 |
| No Improvement | 3 (30%) | 9 (90%) | P = 0.002 |

***Table 2:*** *Histological Improvement among both groups.*

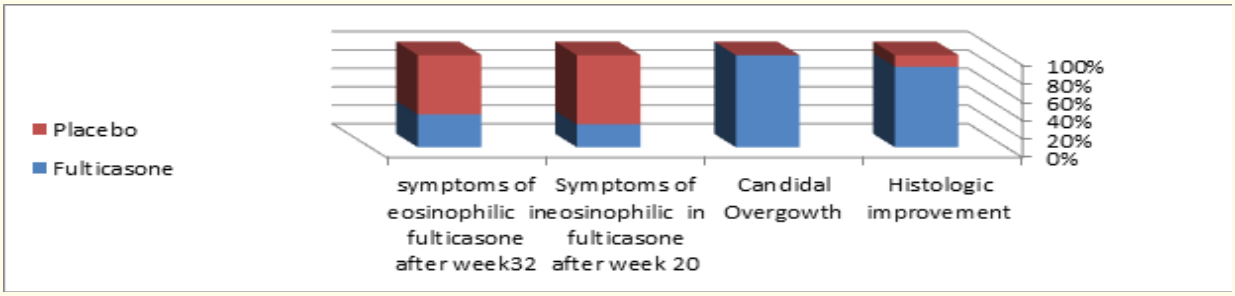


***Figure1:*** *Histological Improvement and side effects among both groups.*

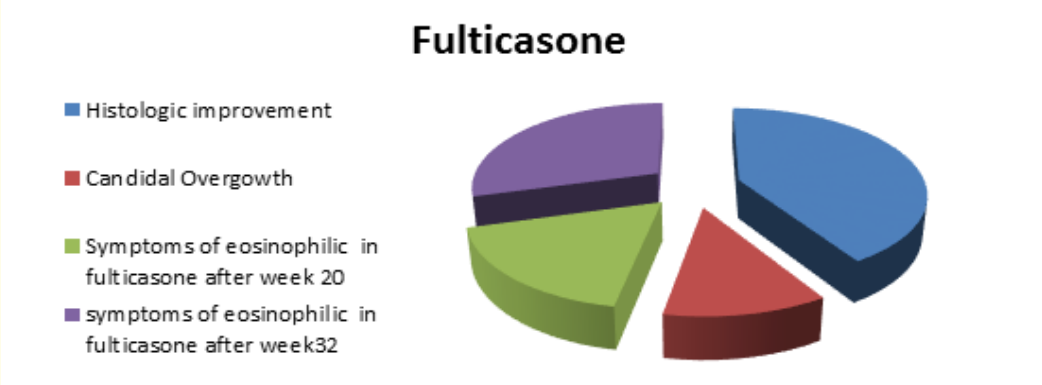


***Figure 2:*** *Histological Improvement and side effect among Fluticasone Group Patients.*

## Discussion

Eosinophilic Oesophagitis is a chronic, immune / antigen mediated, esophageal disease may be isolated gastrointestinal disorder or part of a group of disorders known as the eosinophilic gastrointestinal diseases [19]. The exact etiology of EO is not fully understood. It has been theorised that infiltration of eosinophils into the oesophageal mucosa is the manifestation of allergic eosinophilic gastroenteritis, or is this condition associated with reflux disease. Although response to steroids has been significant in some patients, as it was in our patient group, they do not have the other signs of EoE, so the two pathologies may not be linked, as previously mentioned. It is also very clear that these patients do not respond well to acid suppression therapy [20,21].

The pathogenesis of EoE is related to hypersensitivity reaction in which both IgE-mediated and non-IgE-mediated immune mechanisms are involved. Some studies showed that increased mucosa permeability may allow contact with allergens leading to immunologic response [3]. EoE tends to be a chronic disorder with intermittent or persistent symptoms, Dysphagia, Odynophagia, food Impaction, GERD unresponsive to medical or surgical therapy, abdominal Pain, vomiting, anorexia and early satiety may be the GI complain which are not ameliorated by acid blockade with PPI. Due to its unspecific esophageal symptoms, clinical suspicion is critical in the diagnosis of EoE. Nevertheless, multiple biopsies should be taken from the upper and lower oesophagus at least, 15 intraepithelial eosinophil /HPF must be recognized. Additional histological features may include eosinophilic micro- microabscesses [4].

Our study confirms the utility of FP in adults. It has been used successfully in children [22]. A recent study found that not all adult patients respond to FP. All patients in our study had some degree of histologic and symptomatic improvement on FP, even those with the allergic variant. Importantly, 7 patients had complete resolution of esophageal eosinophilia. However, 30% of patients had experienced

some symptom recurrence after completing treatment with FP. The tolerability of FP was shown by the desire of most of the patients to continue with FP treatment [23]. We recommend swallowed FP as the initial corticosteroid of due to its more favorable side-effect profile [24].

## Conclusion

The use of ingested fluticasone showed improvement of symptoms, and histological pattern. However, due to the low incidence, our sample size was small so we recommend taking oesophageal biopsies in all dysphagia cases. This should be part of the standard protocol for investigation of these patients and the only way that the diagnosis of EoE can be made.

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