

Research Article

Food oral immunotherapy and eosinophilic esophagitis: Complication or comorbidity?

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Abstract

Oral immunotherapy (OIT) is a treatment for immunoglobulin E-mediated food allergy (IgE-FA) where patients consume increasing amounts of food they are allergic to, reducing sensitivity. Allergens treated with OIT include cow milk (CM), egg, and lipid transfer protein (LTP). LTPs are the primary cause of food allergy in adults in Mediterranean European countries. OIT carries risks such as Eosinophilic esophagitis (EoE), a chronic antigen-mediated disease with symptoms of esophageal dysfunction and at least 15 eosinophils/high power field) when other causes of eosinophilia excluding. In children and adults, more information on OIT and EoE is necessary. Aims. To determine the prevalence, evolution, and therapy of EoE in patients with CM, egg, and LTP-OIT. Methods. Prospective observational study with cow milk and egg-OIT (2011-2022) and LTP-OIT (2019-2022) Results We have performed OIT in 344 patients: 104 with milk, 163 with eggs, and 77 with LTP. 10 patients have developed EoE during the maintenance phase; of these, 10 patients with EoE, 6 had treatment OIT (cow's milk), and 4 with OIT (egg), and we have not diagnosed any patients who developed EoE during OIT with LTP. All patients were dysphagia, and 3 were choking. In conclusion, the general prevalence of EoE associated with OIT is 2.9%, but it varies according to the food used. The prevalence of 5.8% EoE by CM-OIT, 2.5% EoE by egg-OIT, and LTP-OIT is null. So, if an EoE is diagnosed during OIT, we recommend agreeing to the therapy with the patient, given that it may be a complication or comorbidity.

Keywords: Cow milk; Eosinophilic esophagitis; Egg; Lipid transfer proteins; Oral immunotherapy

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Abbreviations

OIT: Oral immunotherapy.

IgE-FA: Immunoglobulin E-mediated food allergy.

CM: Cow milk

LTP: Lipid transfer protein.

EoE: Eosinophilic Esophagitis.

CM-OIT: Cow Milk-Immunotherapy

Egg-OIT: Egg-Immunotherapy

LTP-OIT: Lipid transfer protein-Immunotherapy

LP: Latency period

STF: Swallowed topical fluticasone

Introduction

Oral immunotherapy (OIT) is a treatment for immunoglobulin E-mediated food allergy (IgE-FA) where patients gradually consume increasing amounts of food they are allergic to, reducing sensitivity [1]. Common allergens treated with OIT include cow milk (CM), egg, and lipid transfer protein (LTP) [2,3].

LTPs are the primary cause of food allergy in adults in Mediterranean European countries [3].

OIT carries significant risks of allergic reactions and other adverse effects [1,4], such as Eosinophilic esophagitis (EoE). EoE is a chronic antigen-mediated disease characterized by symptoms of esophageal dysfunction and histologically by at least 15 eosinophils/high power field) when other causes of eosinophilia are excluded [5].

In children and adults [4], more information on OIT and EoE is necessary. Aims: to determine the prevalence, evolution, and therapy of EoE in patients with CM, egg, and LTP-OIT.

Methods

Prospective observational study with CM and egg-OIT (2011-2022) and LTP-OIT (2019-2022). Patients with OIT did not have previous symptoms of esophageal dysfunction, and they were diagnosed with EoE during OIT according to current guidelines.

The CM and egg-OIT were always done with these foods, while the LTP-OIT, the initial phase, was done with peach sublingual immunotherapy (Alk laboratory, Madrid -Spain-), and the maintenance phase with commercial juice peach Granini® (50 µg/mL).

Variables studied: age, IgE-mediated allergy to milk, eggs, or vegetables and sensitization by skin prick tests or specific IgE to proteins of those foods, the latency period (LP) between the onset of OIT and stars of the symptoms, phase of OIT in which symptoms appeared, diagnosis, therapy, and evolution of EoE.

This study was carried out according to the Declaration of Helsinki and was approved by the Clinical Research Committee of the hospital. Previously, we obtained informed consent in writing from the patients or their guardians to publish their data. The SPSS Statistics software version 26 (IBM Corp, Armonk, US) was used. Categorical variables were described with percentages.

Results

We have performed OIT in 344 patients: 104 with milk, 163 with eggs, and 77 with LTP. 10 patients have developed EoE during the maintenance phase; of the 10 patients with EoE, 6 had treatment OIT (cow's milk) and 4 with OIT (egg), and we have not diagnosed any patient who has developed EoE during OIT with LTP (Figure 1).

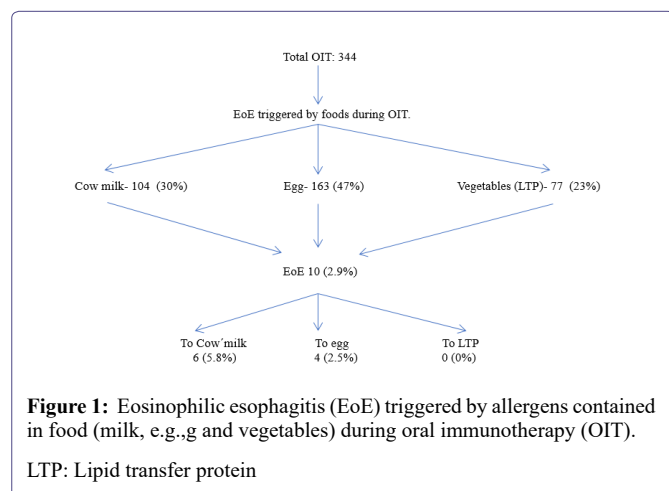


Figure 1: Eosinophilic esophagitis (EoE) triggered by allergens contained in food (milk, e.g.,g and vegetables) during oral immunotherapy (OIT).

LTP: Lipid transfer protein

8 patients were <14 years old, and the remaining two had 17 and 28 years old (one with CM-OIT and the other with OIT with whole egg, white, and yolk). The LP between the onset of OIT and the diagnosis of EoE oscillated from 9 to 19 months in patients with CM-OIT. The 4 patients with egg-OIT were diagnosed with EoE between 29 and 54 months after this therapy.

All patients were dysphagia, and 3 were choking. One patient with OIT with milk tolerated 200 ml; the rest only tolerated 75-200 ml. Of the 4 patients with OIT with eggs, only one tolerated half an egg. Of those who had LTP-OIT, only 3 did not tolerate the vegetable with which they had symptoms.

The first four patients with CM-OIT had their milk withdrawn, and remission of EoE was confirmed clinically and histologically. The other two patients continued with CM-OIT, they responded to Omeprazole and swallowed topical fluticasone (STF), respectively, and we do not know what food triggered their EoE. Of the 4 patients with egg-OIT, only one with E-OIT (white and yolk) remitted the EoE with an egg-free diet. In another patient with a food elimination diet, we detected that the trigger was CM; in the other 2 patients, we did not know the trigger food (both patients are in remission with (STF)).

Discussion

Evidence suggests that OIT could be a risk for the development of EoE. Although, EoE pathogenesis is thought to be IgE-independent. EoE triggered by OIT could act through IgE to cause inflammation esophageal [6].

In 2014, EoE during OIT was 2.7% [7]. In our study, the global prevalence of EoE during OIT is 2.9%. The prevalence of EoE in

CM-OIT is 5.8%, egg-OIT is 2.5%, and LTP-OIT is 0%. These differences could be because the CM is the food triggering EoE with more frequency, and EoE triggered by LTP-OIT has yet to be described. EoE has been reported as a milk, egg, and peanut OIT complication [8]. Also, EoE is probably a comorbidity in FA patients undergoing OIT since in a study of more 12 000 FA children, 4.7% developed EoE without OIT [9].

The true incidence and prevalence of EoE during OIT may vary, depending on the definition of EoE. In addition, the long-term effect of OIT on EoE is unknown.

In our study with children and adults, the global prevalence of EoE during OIT with egg and milk is higher than in another study published only in children on the prevalence of EoE in patients with OIT. In both studies, EoE was diagnosed in the maintenance phase. In both studies, the prevalence of EoE was higher in the CM-OIT than with egg-OIT [10].

We ask ourselves, why, during 4 years with LTP-OIT, have we not diagnosed any EoE? During the initiation phase of LTP-OIT, the patients spit it out. In the maintenance phase, swallow it. Later, patients consume LTP daily in any vegetable food [3]. The difference is that the CM and egg-OIT were with animal proteins in children, and LTP-OIT was with vegetable proteins in adults. Here are no studies of EoE and LTP-OIT in children.

This study has limitations since it is Unicenter, and we did not perform an endoscopy before OIT started. Still, it has the strength to be a prospective study, and there are no studies on the association of LTP-OIT and EoE. In conclusion, the general prevalence of EoE associated with OIT is 2.9%, but it varies according to the food used. The prevalence of 5.8% EoE by CM-OIT, 2.5% EoE by egg-OIT, and LTP-OIT is null. So, if an EoE is diagnosed during OIT, we recommend agreeing to the therapy with the patient, given that it may be a complication or comorbidity.

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Declaration of conflict of interest

All authors who have contributed to this work declare that they have NO conflicts of interest.

Author's contribution

Gratacos Gomez and Gomez Torrijos conceived the study, wrote the protocol, recruited the bibliography, and thoroughly reviewed the manuscript before submitting it.

Martin Iglesias and Bracamonte was responsible for the recruitment and clinical evaluations of the patients.

Meneses Sotomayor and Borja Segade wrote this manuscript and translated it into English after it was reviewed and approved by all the authors.

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