Allergol Immunopathol (Madr). 2016;xxx(xx):xxx-xxx

Allergologia et immunopathologia

Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica

www.elsevier.es/ai

ORIGINAL ARTICLE

Primary eosinophilic gastrointestinal disorders in children who have received food oral immunotherapy

L.Á. Echeverría-Zudaire[a,*], S. Fernández-Fernández[b], A. Rayo-Fernández[b], C. Muñóz-Archidona[c], R. Checa-Rodriguez[d]

[a] *Pediatric Allergy Unit, Severo Ochoa Universitary Hospital, Leganés, Spain*
[b] *Pediatric Gastroenterology Unit, Severo Ochoa Universitary Hospital, Leganés, Spain*
[c] *Pediatric Allergy Unit, Villalba General Hospital, Villalba, Spain*
[d] *Pediatric Gastroenterology Unit, Rey Juan Carlos Universitary Hospital, Móstoles, Spain*

Received 30 December 2015; accepted 4 May 2016

KEYWORDS
Eosinophilic esophagitis;
Food oral immunotherapy;
Eosinophilic gastroenteritis;
Eosinophilic colitis;
Food allergy;
Desensitization;
Immunologic or immune tolerance

Abstract
Background: Food oral immunotherapy (OIT) involves the administration of the food allergen causing the symptoms, in order to induce tolerance. Primary eosinophilic gastrointestinal disorders (PEGDs) are characterised by an eosinophil-rich inflammation affecting different locations of the digestive tract. We present a series of patients with PEGDs in a group of children following OIT with milk and/or egg.
Material and methods: A prospective study during the period 2006–2014 was performed in paediatric patients subjected to OIT with milk and/or egg. When these children present persistent gastrointestinal symptoms, they are referred to the Paediatric Gastroenterology Unit for evaluation.
Results: Primary eosinophilic gastrointestinal disorders were diagnosed in eight of the 128 cases of OIT (6.25%). The time to PEGDs development was variable: two cases showed symptoms during OIT, and the rest with a median time of 29 months (15–48 months). Food treatment discontinuation was not required in four of the five cases of eosinophilic oesophagitis, although food removal was necessary in patients with eosinophilic gastroenteritis.
Conclusions: We report the highest prevalence of PEGDs in children subjected to OIT, and the first cases of eosinophilic gastroenteritis following food OIT.

The monitoring of new digestive signs and symptoms after OIT is crucial for the diagnosis of these disorders, and prolonged follow-up is required. The management of such patients and the need or not to eliminate the food should be assessed on an individualised basis, according to the severity of the condition, its evolution and response to different treatment alternatives.

* Corresponding author.
E-mail address: lecheverria333@gmail.com (L.Á. Echeverría-Zudaire).

http://dx.doi.org/10.1016/j.aller.2016.05.002
0301-0546/

Introduction

The prevalence of food allergy in childhood is high, with a negative impact upon general perceived health, family and social activities, and quality of life of both patients and their families. Current treatment strategy in such cases is to strictly avoid the offending food, provide rescue medication to control the adverse reactions caused by transgressions, and afford adequate patient education. Despite such measures, however, food allergy remains one of the most frequent causes of anaphylactic reactions in children and young adults.[1–3]

Food oral immunotherapy (OIT) involves the administration of increasing doses of the food to which the patient is allergic, with the aim of reducing the symptoms associated to natural exposure (desensitisation) and, if possible, achieve permanent tolerance. Food oral immunotherapy may be regarded as an alternative to elimination diets in patients with IgE-mediated allergy that maintain clinical reactivity beyond the age when natural tolerance is usually reached.[3–5] The technique is fundamentally used with cow's milk and egg, since in our setting it is difficult to successfully avoid these foods, and transgressions are frequent and can be serious.[6,7] Although death as a result of anaphylaxis is infrequent in such cases, the risk must not be underestimated – particularly in adolescents and asthmatic individuals.

Published studies to date indicate that OIT is able to achieve desensitisation to cow's milk and egg in 84% and 81% of the patients, respectively.[8–10] However, the ability of OIT to induce permanent or sustained tolerance has not, to date, been extensively evaluated. The procedure is not without risks, and prolonged maintenance treatment is required. It therefore must be accepted by the patient and/or family, after receiving adequate information about the treatment.

Primary eosinophilic gastrointestinal disorders (PEGDs) are a heterogeneous group of diseases characterised by an eosinophil-rich inflammation affecting different locations of the digestive tract: eosinophilic oesophagitis (EoE), eosinophilic gastroenteritis (EoGE) (gastritis/enteritis) and eosinophilic colitis (EoC). Eosinophilic oesophagitis is the most common form, and is a chronic oesophageal disorder of immune origin, mediated by antigens and clinically and histopathologically characterised by oesophageal dysfunction and a predominantly eosinophilic infiltration ($\geq$15 eosinophils per high-power microscopy field (eos/hpf)). Eosinophilic oesophagitis mainly affects males and is typically associated to other allergic disorders such as asthma and atopic dermatitis. Although the underlying aetiopathogenesis is not clear, mainly food allergens and inhaled aeroallergens to a lesser extent are known to play an important role in the development of the disease.[11–13]

Although the development of PEGD after OIT has been described in the recent literature, the relationship between them remains controversial. All available publications refer to sporadic cases of EoE.[14–19] Recently, Lucendo et al. have published a systematic review and meta-analysis demonstrating a prevalence of EoE after OIT of 2.7%.[20] There are no published cases of EoGE and EoC after food OIT.

Objective

The present study aims to describe the incidence and characteristics of PEGDs manifested in a prospective group of children with persistent IgE-mediated food allergy undergoing to OIT with milk and/or egg.

Material and methods

A prospective study during the period 2006–2014 was performed in paediatric patients subjected to OIT with milk and/or egg due to persistent allergy to these foods as demonstrated by clinical findings, prick testing, specific-IgE quantification and a positive open oral food challenge. During both phases, an initial dose escalation and maintenance phase, strict monitoring of new gastrointestinal signs and symptoms was carried out (eating problems, vomiting, weight loss, abdominal pain, chest pain, burning sensation, persistent diarrhoea, dysphagia of oesophageal food impaction). None of the patients presented digestive symptoms before starting the OIT. When such children presented persistent gastrointestinal symptoms, they were referred to the Paediatric Gastroenterology Unit for evaluation and they were first clinically evaluated, and if PEGDs was suspected then digestive endoscopy was performed and biopsy specimens obtained.

Eosinophilic gastroenteritis involves selective eosinophilic infiltration of the stomach and small and/or large intestine, in the absence of other possible causes of eosinophilia of the digestive tract. It is characterised by variable involvement of the layers of the gastrointestinal wall, with different degrees of infiltration and spread which will change the associated symptoms (eosinophilic gastroenteritis is defined by eosinophil-predominant inflammation in one or more of the following locations: $\geq$10–30 eos/hpf in the stomach and small intestine and $\geq$70 eos/hpf in the large intestine). On the other hand, eosinophilic colitis is defined as eosinophilic infiltration limited to the colon, in the absence of other possible causes of eosinophilia. The aetiopathogenesis of both, EoGE and EoC is even less well known than that of EoE, although an underlying allergic mechanism has also been suggested, and the condition sometimes improves when an elimination diet is introduced.[21–23]

Statistical analysis

Proportions were expressed as percentages and 95% confidence intervals (CI). Continuous variables were presented as mean $\pm$ standard deviation.

Results

In the period 2006–2014, our Paediatric Allergy Unit applied the OIT protocol in 97 cases with cow's milk and 31 cases with egg. In that period, PEGDs were diagnosed in eight of the global 128 cases of OIT representing 6.25% of the sample (95% CI: 2.05–10.4%). Most of the affected patients were males between 3 and 14 years of age. Eosinophilic oesophagitis was diagnosed in six patients with exclusively

Please cite this article in press as: Echeverría-Zudaire LÁ, et al. Primary eosinophilic gastrointestinal disorders in children who have received food oral immunotherapy. Allergol Immunopathol (Madr). 2016. http://dx.doi.org/10.1016/j.aller.2016.05.002