
Food Protein–Induced Enterocolitis Syndrome in an Adult Population From Spain

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Acute food protein-induced enterocolitis syndrome (FPIES) is a non-IgE-mediated condition involving gastrointestinal hypersensitivity to food that is characterized by profuse vomiting 1-4 hours after ingestion. It may be accompanied by pallor, lethargy, hypotension, and hypothermia [1]. Although classically considered a pediatric disorder, several reports in adults have been published since 2012 [2-8].

Our aim was to describe the clinical features of acute FPIES in Spanish adults by comparing our findings with those previously published on adult and pediatric populations.

We performed a retrospective chart review of patients referred to our outpatient allergy unit from 2017 to 2020 because of clinical manifestations compatible with FPIES. Patients underwent skin prick tests (SPTs) with commercial extracts (ALK Abelló) and prick-by-prick tests with fresh food and total and specific IgE (ImmunoCAP, Thermo Fisher).

SPT and open food challenge (OFC) were performed every 2-3 years to evaluate tolerance to the offending food. OFC was performed over 2 days. On the first day, 30% of a food portion was offered, and if there was no reaction, the patient was asked to have the complete portion on the second day. Patients remained under observation for 4 hours afterwards. Orodispersible ondansetron was administered in the case of clinical manifestations.

The study was approved by the Galician Medical Research Ethics Committee (registration code 2021/115).

Of the 28 adults included, 21 were women and 7 men; mean (range) age was 39.82 (17-65) years. Only 1 adolescent was included (age, 17 years).

Thirteen patients had allergic rhinoconjunctivitis to airborne allergens, and 1 was allergic to egg and milk during childhood.

Mean age at the first reaction was 32.07 (15-60) years. The average number of reactions before achieving the diagnosis was 5.79 (3-10).

All patients presented with repetitive vomiting 1 to 4 hours after food ingestion. Twenty-five also experienced abdominal pain and developed diarrhea during the following 24 hours. Sixteen patients had pallor and lethargy. Mean latency time between food ingestion and the onset of symptoms was 137.14 (60-240) minutes.

The most frequently involved foods were seafood (11 bivalves, 3 crustaceans) followed by fish (2 hake, 1 salmon, 1 sole).

Only 2 patients developed symptoms after eating foods from different groups (fish and bivalves).

One patient presented serum specific IgE to cow's milk (1.09 kU/L), and another patient had a positive SPT result with salmon and clams.

Analysis of the follow-up revealed that none of the 7 patients who agreed to undergo OFC tolerated the offending food and had been avoiding it for at least 5 years.

Table. Demographic and Clinical Characteristics of Adult Patients With Food Protein-Induced Enterocolitis Syndrome

Characteristics	Value
Sex, No. (%)	
Men	7 (25)
Women	21 (75)
Median (IQR) age at first reaction, y	32.07 (15-60)
Median (IQR) age at diagnosis, y	39.82 (17-65)
Median delay to diagnosis, y	7.75
Median (IQR) no. of reactions prior to diagnosis	5.79 (3- >10)
Symptoms, No. (%)	
Vomiting	28 (100)
Abdominal pain	25 (89)
Diarrhea	25 (89)
Pallor	16 (57)
Lethargy	16 (57)
Median (IQR) latency period, min	137.14 (60-240)
Food involved, No. (%)	
Bivalves	11 (39)
Crustacean	3 (10.7)
Fish	4 (14.8)
Egg	3 (10.7)
Cow's milk	1 (3.5)
Banana	1 (3.5)
Peanut	1 (3.5)
Veal	1 (3.5)
Food groups involved, No. (%)	
1	26 (92.8)
2 (fish and seafood)	2 (7)
Atopy, No. (%)	
Rhinoconjunctivitis	13 (46.4%)
Grass pollen	5 (17.8)
Mites	11 (39)
Food allergy (egg and cow's milk)	1 (3.5%)

One of the patients who reacted to boiled egg tolerated its baked version.

Demographic and clinical data are summarized in the Table.

Although vomiting was the most frequent presentation in our series, abdominal pain has been reported by most authors as the main symptom of adult FPIES [4-6], in contrast to children. Since adult patients do not meet the proposed diagnostic criteria [9], Vazquez-Ortiz and Infante [10] recently proposed considering abdominal pain instead of vomiting as the major criterion for acute FPIES in adults.

In agreement with previous reports [4-8], we found a predominance of female adult patients, while in pediatric FPIES, more than half of the affected children are boys [1].

Given the poor specificity of the clinical manifestations of FPIES and the absence of diagnostic biomarkers, diagnostic delay is common [5,7,8,11,12]. In adults, Li et al [8] reported a median of 10 years from symptom onset to diagnosis, similar to the 8-year delay reported by Gonzalez-Delgado et al [5]. The patients we studied experienced 3 to 10 reactions before FPIES was diagnosed.

We found that seafood was the main culprit, as described previously in series from Australia, Spain, and Canada [4-8]. Regarding the Spanish population, we found that mollusks, specifically bivalves, were involved in most cases, in agreement with Crespo et al [7]. The second most frequently responsible food in our population was fish, as previously reported for Spanish adults [5,7]. In Canada, the second most frequent culprit after seafood was dairy products [6], and in Australia [4] egg and fish. In children, cow's milk is the main cause of FPIES worldwide [1], although geographic differences have been found for solid foods [11-14]. More studies in adults are needed to determine whether geographical origin also influences the predominance of a particular solid food.

In our series, only 2 patients (7%) reacted to 2 different food groups, ie, fish and bivalves in both cases; this percentage is lower than the 20% reported by González-Delgado et al [5], the 16% reported by Tan and Smith [4], and the 30% reported by Du et al [6], and similar to the 10% reported by Crespo et al [7]. Fish and seafood (mollusks and crustaceans) was the most common association found in those studies.

Even if FPIES is not IgE-mediated, increased rates of atopic manifestations have been reported in affected children [1,11]. There are discrepancies regarding atopic comorbidities in adults with FPIES. Half of the patients we studied had an atopic background. Higher percentages were reported by González-Delgado et al [5] and Tan and Smith [4]. In contrast, only 3 out of 19 adult patients had a history of atopy in the series published by Li et al [8].

As observed for Spanish and Italian children [1], no or low percentages of atypical FPIES have been reported for adults [4-7]. Only 2 of the 28 patients included in the present study had detectable food-specific IgE.

In children, the time to tolerance of the offending food varies depending on the food involved. FPIES induced by solid foods, especially fish, seems to have a more protracted course than FPIES induced by cow's milk or rice [1]. In adults, we lack data on the natural course of FPIES, although, as we

observed, most reports suggest a more prolonged course of FPIES in adults than in children [5,7].

In summary, adult FPIES is not such a rare disorder and differs little in clinical and epidemiological terms from pediatric FPIES. Seafood is the most frequently involved food. More studies are needed to understand the natural history of FPIES in this cohort of patients.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

- Vila Sexto L. Latest insights on food protein-induced enterocolitis syndrome: An emerging medical condition. *J Investig Allergol Clin Immunol*. 2018;28(1):13-23.
- Fernandes BN, Boyle RJ, Gore C, Simpson A, Custovic A. Food protein-induced enterocolitis syndrome can occur in adults. *J Allergy Clin Immunol*. 2012;130(5):1199-2000.
- Zubrinich C, Hew M, O'Hehir R. Egg provoked food protein-induced enterocolitis-like syndrome in an adult. *Clin Case Rep*. 2016;4(9):899-901.
- Tan JA, Smith WB. Non-IgE-mediated gastrointestinal food hypersensitivity syndrome in adults. *J Allergy Clin Immunol Pract*. 2014;2(3):355-7.
- González-Delgado P, Caparrós E, Moreno V, Cueva B, Fernández J. Food protein-induced enterocolitis-like syndrome in a population of adolescents and adults caused by seafood. *J Allergy Clin Immunol Pract*. 2019;7(2):670-2.
- Du Y, Nowak-Węgrzyn A, Vadas P. FPIES in adults. *Ann Allergy Asthma Immunol*. 2018;121(6):736-8.
- Crespo J, Skrabski F, Pérez-Pallise ME, De Castro-Martínez FJ, Zubeldia JM, Infante S. Relevant features of adult-onset food protein-induced enterocolitis syndrome. *J Allergy Clin Immunol Pract*. 2021 Apr;9(4):1759-60.
- Li DH, Wong-Pack A, Macikunas AL, Kim H. Adults with possible food protein-induced enterocolitis syndrome with crustacean ingestion. *Allergy Asthma Clin Immunol*. 2020 Nov 11;16(1):99.
- Nowak-Węgrzyn A, Chehade M, Groetch ME, Spergel JM, Wood RA, Allen K, et al. International consensus guidelines for the diagnosis and management of food protein-induced enterocolitis syndrome: Executive summary—Workgroup Report of the Adverse Reactions to Foods Committee, American Academy of Allergy, Asthma & Immunology. *J Allergy Clin Immunol*. 2017;139(4):1111-26.
- Vazquez-Ortiz M, Infante S. Diagnostic criteria for food protein-induced enterocolitis syndrome. Can do we better? *Ann Allergy Asthma Immunol*. 2021;126:458-9.
- Vila L, García V, Rial MJ, Novoa E, Cacharron T. Fish is a major trigger of solid food protein-induced enterocolitis syndrome in Spanish children. *J Allergy Clin Immunol Pract*. 2015;3(4):621-3.
- Ruffner MA, Ruymann K, Barni S, Cianferoni A, Brown-Whitehorn T, Spergel JM. Food protein-induced enterocolitis syndrome: insights from review of a large referral population. *J Allergy Clin Immunol Pract*. 2013;1(4):343-9.
- Miceli Sopo S, Giorgio V, Dello Iacono I, Novembre E, Mori F, Onesimo R. A multicentre retrospective study of 66 Italian children with food protein-induced enterocolitis syndrome: different management for different phenotype. *Clin Exp Allergy*. 2012 Aug;42(8):1257-65.
- Mehr S, Frith K, Barnes EH, Campbell DE, FPIES Study Group. Food protein-induced enterocolitis syndrome in Australia: A population-based study, 2012-2014. *J Allergy Clin Immunol*. 2017 Nov;140(5):1323-30.

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