

NON-IGE MEDIATED FOOD ALLERGY

Food Protein–Induced Enterocolitis Syndrome Food Challenges: Experience From a Large Referral Center

Wang KY, Lee J, Cianferoni A, et al. *J Allergy Clin Immunol Pract.* 2019;7(2):444–450

PURPOSE OF THE STUDY: To describe experience with oral food challenges (OFCs) for food protein-induced enterocolitis syndrome (FPIES), using a protocol that includes ingestion of one-third of the goal food serving size with 4 hours of observation, followed by home titration to goal dose.

STUDY POPULATION: A total of 119 subjects underwent 169 OFCs at Children's Hospital of Philadelphia to 19 different foods between 2014 and 2017. Patients with food protein-induced allergic proctocolitis were excluded. Patients with intermittent food exposures and delayed emesis within 1 to 4 hours and/or diarrhea within 5 to 10 hours were classified as having acute FPIES. Patients with daily ingestion of the food with intermittent emesis, chronic diarrhea, poor weight gain, or malnutrition were classified as having chronic FPIES.

METHODS: This was a retrospective chart review. Data regarding age, sex, implicated foods, age of onset, and symptoms prompting food challenge were collected. OFC data were also collected, including age at the time of challenge, cumulative dose of food, outcome of challenge, timing to reaction, treatment of positive challenge results, disposition, and presence of a late reaction.

RESULTS: Thirty OFCs (18%) resulted positive, with 17 (10%) resulting positive during the initial challenge and 13 (7.7%) during home dosing. Most reactions during initial OFC required intravenous fluids (IVFs). Two patients developed hypotension. In 139 OFCs (82%), patients tolerated both initial OFC and home dose titration. One hundred twenty six OFCs (75%) were performed in patients with a previous history of FPIES reaction to the index food, and 43 OFCs (25%) were performed to foods avoided as a precaution. In all positive OFC results, symptoms of acute FPIES reaction occurred at least 85 minutes after dosing. Of all OFCs performed, IVF was administered to 14 patients (7.1%), and ondansetron was administered to 12 patients (6.1%). The mean age of passing an OFC to milk, soy, and grain was lower than that of other solid foods. The mean age of passing an OFC to milk was 35 months, soy was 38.4 months, and grains were 35.7 months.

CONCLUSIONS: This FPIES OFC protocol is safe. Early administration of IVFs may prevent the development of hypotension. It is difficult to stratify the risk of a severe or delayed reaction on the basis of patient characteristics. More data are needed to identify patients appropriate for home food introduction.

REVIEWER COMMENTS: Risk stratification based on patient histories is challenging. In the studied population, there

was overlap of clinical features between patients who required IVFs and those who were able to orally rehydrate in the context of a positive OFC result. Data from this single-center referral center for FPIES are encouraging and suggest potential for home food reintroduction in older patients. Data regarding the mean age of successful reintroduction for various foods in this study may help to inform future studies.

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Food Protein-Induced Enterocolitis Syndrome: Data From a Multicenter Retrospective Study in Spain

Díaz JJ, Espín B, Segarra O, et al; Gastrointestinal Allergy Working Group of the Spanish Society of Pediatric Gastroenterology, Hepatology and Nutrition (SEGHPN). *J Pediatr Gastroenterol Nutr.* 2019;68(2):232–236

PURPOSE OF THE STUDY: To describe the clinical presentation and management practices of food protein-induced enterocolitis syndrome (FPIES).

STUDY POPULATION: The study included 120 patients (0.5 months to 12 years of age) diagnosed with FPIES in 2017 across 37 hospitals in Spain.

METHODS: This study involved a retrospective chart review of patients diagnosed with FPIES using the 2017 international consensus criteria. Age, clinical symptoms, implicated foods, oral food challenge, laboratory values, skin prick testing, number of episodes before diagnosis, and management approach were collected and analyzed for comparison.

RESULTS: The researchers in this study demonstrated that 92.5% ($n = 111$) of FPIES cases had an acute presentation (2–4 hours), with the majority (76.7%) considered mild to moderate in severity. The most common food trigger was cow's milk (36.7%), followed by fish (32.5%), hen's egg (10.8%), and rice (10%). Acute FPIES frequently presented with vomiting (100%), pallor (89.2%), and lethargy (88.3%); whereas chronic FPIES presented with diarrhea (77.8%) or bloody stools (44%). Although 96% of the study population had immunoglobulin E or skin prick testing performed, only 15.7% of patients had positive test results. The acute management of FPIES involved intravenous fluids (46.7%), ondansetron (34.2%), and intravenous corticosteroids (5%). Additionally, extensively hydrolyzed formula was used in 69.8% of cow's milk FPIES cases, whereas amino acid-based formulas were used in 20.5%. Interestingly, 50% of rice FPIES had a severe course compared with 20% for cow's milk, 21% for fish, and 7.6% for hen's egg ($P = .032$). Delays in diagnosis

were common, with 58.5% of patients having at least 2 to 3 episodes before diagnosis. Median age of diagnosis for cow's milk FPIES was 5 months of age, in contrast to fish and hen's egg (14.5 and 13.8 months, respectively).

CONCLUSIONS: FPIES requires further characterization and standardization of practice management. In this expansive description of FPIES in a multicenter Spanish cohort, cow's milk remained the most common trigger, but fish and egg were also recognized as important triggers.

REVIEWER COMMENTS: This is the largest European FPIES series published using recent international criteria for diagnosis. This observational study demonstrates the gaps in standardization of diagnosis and management. This study also suggests cultural and dietary factors may affect disease presentation because fish is rarely a trigger for FPIES in the United States, whereas it is the second most common trigger in Spain. This study also highlights the need for future reports to identify risk factors and non-invasive biomarkers to improve diagnostic delays.

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Phenotypic Characterization of Eosinophilic Esophagitis in a Large Multicenter Patient Population From the Consortium for Food Allergy Research

Chehade M, Jones SM, Pesek RD, et al. *J Allergy Clin Immunol.* 2018;6(5):1534–1544

PURPOSE OF THE STUDY: To describe the clinical, endoscopic, and histopathologic features of a large number of children and adults with eosinophilic esophagitis (EoE) across the United States. This would allow for a more accurate definition of phenotypes across age groups and discovery of potential disease associations that would not be possible otherwise.

STUDY POPULATION: The population included 705 subjects ages 6 months to 65 years with confirmed EoE enrolled at 5 different study sites in the United States.

METHODS: Registry was part of a study conducted by the Consortium of Food Allergy Research with the primary aim to establish the genetic basis of EoE. Uniform questionnaires were used at all sites to gather information on demographics, medical and surgical history, and family history. Data on endoscopic findings and histopathology were collected at each site. Analyses of the data were primarily descriptive.

RESULTS: Median age at diagnosis was 8 years, and median age at symptom onset was 5 years. Older age was associated with a longer delay between symptom onset and diagnosis. White participants had a longer time from symptom onset to diagnosis compared with nonwhite participants.

A history of food allergy or atopic dermatitis was associated with a significantly shorter time gap between symptom onset and diagnosis. High rates of food allergies to uncommon foods, such as beef, poultry, and corn, were noted in all age groups. Children had more abdominal pain and emesis than adults, whereas adults had more heartburn, chest pain dysphagia, and food impaction. Food allergies, food-induced anaphylaxis, asthma, and allergic skin disorders were more common in children and in nonwhite participants, but allergic rhinitis and conjunctivitis did not differ by age. Family members had a higher incidence of atopic diseases, EoE, gastroesophageal reflux disease, eosinophilic gastrointestinal disorders, and autoimmune disorders.

CONCLUSIONS: This multicenter study allowed for a heterogeneity of subjects that resulted in a number of findings that have not been noted in smaller studies: (1) gastrointestinal eosinophilia at a site contiguous to the esophagus occurs in 5% of patients; (2) there is a large time gap between symptom onset and diagnosis, which is influenced by age and race; (3) symptoms vary with age; (4) symptoms vary with race; (5) failure to thrive is common in children; and (6) infectious and immune disorders are more common in patients and family members.

REVIEWER COMMENTS: This study provides several new observations on EoE, and pediatricians need to be aware of some of the symptoms present in children with this disorder, besides gastroesophageal reflux disease. Recurrent abdominal pain, emesis, and failure to thrive may be presenting features. Consider EoE in patients with food allergies and atopic dermatitis with suggestive histories.

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Specific IgG4 Antibodies to Cow's Milk Proteins in Pediatric Patients With Eosinophilic Esophagitis

Schuyler AJ, Wilson JM, Tripathi A, et al. *J Allergy Clin Immunol.* 2018;142(1):139–148.e12

PURPOSE OF THE STUDY: Although food protein causes eosinophilic esophagitis (EoE), the mechanism is not clear and appears not to be immunoglobulin E (IgE)–mediated. Cow's milk (CM) is among the most common causal foods in patients with EoE. Specific immunoglobulin G4 (sIgG4) antibodies to food extracts, including CM, have been found in sera and esophageal biopsies of adults with EoE. Is this true in children with EoE?

STUDY POPULATION: This study included data from 71 pediatric patients with EoE and 210 pediatric control subjects from an unselected birth cohort (Project Viva).

METHODS: Sera were assayed for sIgG4 and specific IgE to major CM proteins (α -lactalbumin, β -lactoglobulin, and caseins) as well as to wheat, soy, egg, and peanut.