Food Protein-Induced Enterocolitis Syndrome: Insights From Review of a Large Referral Population


PURPOSE OF THE STUDY. The goal of this study was to describe the demographic characteristics, clinical symptoms, and allergy test results in a large cohort of patients with food protein–induced enterocolitis syndrome (FPIES).

STUDY POPULATION. Patient charts were reviewed from The Children’s Hospital of Philadelphia, a large referral hospital with patients primarily from Pennsylvania, New Jersey, and Delaware.

METHODS. This study was a retrospective chart review of electronic medical records from 2007 to 2012. Originally, 992 patients were identified as having “allergic gastroenteritis and colitis” according to International Classification of Diseases, Ninth Revision, coding. A total of 462 patients met the classic definition of FPIES with reproducible episodes of prolonged vomiting or diarrhea 2 to 6 hours after exposure to an inciting allergen. Patients with IgE-mediated food allergy and chronic symptoms (eg, chronic diarrhea) were excluded. Patch testing with foods (similar to contact allergy testing performed for nickel allergy) were conducted.

RESULTS. The patient population was primarily male (60%) and white (65%). Milk was the most common trigger food, with reactions reported in 67% of patients. The next most common food trigger was soy (41%), followed by grains (34.6%) and egg (11%). FPIES reactions were less common to meats and fish, vegetables and fruits, and peanut and tree nuts. A majority (70%) of patients reacted to 1 or 2 foods, and 5% reacted to >6 foods. Patients had their first FPIES reaction to milk and soy at ~7 months of age compared with 12 months of age for solid foods. There was a relatively equal distribution between patients who presented with vomiting versus vomiting and diarrhea, and a minority (5%) presented with severe symptoms, including hypotension, pallor, or lethargy. Skin prick test results were negative in 96% of patients tested regardless of the food, and patch test results were negative 45% of the time over all foods. More than 85% of the patients had resolved their FPIES reactions by 5 years of age.

CONCLUSIONS. The data from this study confirm previous findings that a majority of FPIES reactions are due to milk and soy, and most patients experience resolution of this allergy early in life. It also confirms previous findings that results of skin prick tests are typically negative in FPIES. The results refute a previous pilot study that suggested utility of patch tests with foods. FPIES remains a clinical diagnosis with no simple method for testing.

REVIEWER COMMENTS. This study is the largest of FPIES to date. The prevalence of this type of food allergy is unclear. Familiarity with FPIES is important because misdiagnosis is common, considering that symptoms may initially mimic infection or a surgical malady and results of typical allergy tests measuring IgE antibodies are characteristically negative.

Clinical, Serologic, and Histologic Features of Gluten Sensitivity in Children


PURPOSE OF THE STUDY. The goal of this study was to evaluate the characteristics of gluten sensitivity in children.

STUDY POPULATION. The study included 15 children (10 boys, 5 girls) with a median age of 10.3 years (range: 1.6–15 years) who were diagnosed at 2 pediatric gastroenterology tertiary centers in Italy. Patients were referred for excluding an adverse food reaction to wheat.

METHODS. The diagnosis of gluten sensitivity was made after symptoms were associated with wheat ingestion despite a negative celiac disease evaluation. All children included in this case series tested negative for IgA endomysial antibodies, IgA tissue transglutaminase antibodies, wheat-specific IgE, gluten-specific IgE, skin prick testing to wheat, and atopy patch testing to wheat. A small bowel biopsy was offered to all 15 patients (11 of 15 consented). Tissue transglutaminase IgA, endomysial antibody and native antigliadin antibody IgA and IgG, HLA typing, and multiple hematologic measurements were obtained before initiation of a gluten-free diet. Patients followed a gluten-free diet for 8 weeks, followed by an open, hospital-based 5-g gluten challenge and monitoring for 48 hours. Symptom diaries were used. A 30% increase in a symptom score after the gluten challenge was deemed significant. A group of 15 patients with functional gastrointestinal disorders without celiac disease and without food-associated symptoms and 15 patients with celiac disease served as the control and comparison groups, respectively.

RESULTS. The median time to symptom onset after the open gluten challenge was 44 hours (range: 38–80 hours). Abdominal pain was the most frequently reported symptom postchallenge, reported in 12 (80%) of 15 children, followed by diarrhea (73%), fatigue (33%), and bloating (26%). Limb pain, vomiting, constipation, headache, and failure to thrive were also reported. Antigliadin antibody IgG was detected in 10 (66%) of 15 children with a diagnosis of gluten sensitivity, in 13 children (86%) with celiac disease, and in 2 (13%) of the control children. Titers of antigliadin antibody IgG were significantly lower in children with...
gluten sensitivity compared with those with celiac disease ($P < .001$). Antigliadin antibody IgA was detected in 1 child with gluten sensitivity and in 11 children with celiac disease ($P < .001$). HLA-DQ2 was present in all children with celiac disease and in 7 (46%) of the 15 children with gluten sensitivity. Results of small bowel biopsies of gluten-sensitive children revealed 9 (82%) of 11 had normal mucosa, and 2 (18%) of 11 had Marsh stage 1 mucosa (increased intraepithelial lymphocytes).

CONCLUSIONS. Children with gluten sensitivity lack reliable serologic or genetic markers of the disease, as is the case in adults with gluten sensitivity. However, similar to previous observations in adult gluten-sensitive patients, this study found that native antigliadin antibody IgG positivity and presence of HLA-DQ2 are more common in children with gluten sensitivity compared with control subjects.

REVIEWER COMMENTS. Antigliadin antibodies are commonly present in any patient with a disrupted gastrointestinal barrier, and they have actually fallen out of favor in the diagnosis of celiac disease. Thus, antigliadin antibody IgG positivity in nonceliac gluten-sensitive patients should be considered with caution. No biomarker for gluten sensitivity exists, and gluten sensitivity remains a clinical diagnosis. Other studies suggest that fermentable, oligo-, di, monosaccharides and polyols (FODMAPs) may be the symptom-inducing components of wheat, and not gluten itself. Carefully crafted prospective, double-blind studies are needed to further characterize gluten sensitivity and to clarify whether FODMAPs are involved.

Fructose Intolerance/Malabsorption and Recurrent Abdominal Pain in Children

PURPOSE OF THE STUDY. The goal of this study was to determine the incidence of fructose malabsorption in children who present with chronic or recurrent abdominal pain and whether a low-fructose diet improves their symptoms.

STUDY POPULATION. Study participants were recruited after retrospective chart review of consecutive patients from 2007 to 2009 without a specific etiology identified for chronic abdominal pain. A total of 222 children ages 2 to 19 years (64% female) who had been evaluated by a pediatric gastroenterologist for persistent abdominal pain completed the study.

METHODS. All enrolled participants underwent a breath hydrogen test (BHT) after a fructose ingestion dose of 1 g/kg (maximum: 25 g). A breath hydrogen value of $\geq 20$ ppm from baseline was considered positive for fructose malabsorption. These participants, with the aid of a dietitian, underwent a low-fructose diet with subjective follow-up assessment of clinical symptoms.

RESULTS. A total of 121 (55%) of 222 participants had a positive fructose BHT result. All 121 participants completed a 2-month low-fructose diet, with 77% ($P < .0001$) experiencing clinical improvement. Fifty-four percent of the fructose-negative BHT participants reported resolution of symptoms without a low-fructose diet although this finding did not reach statistical significance ($P = .37$).

CONCLUSIONS. Not only is fructose malabsorption a common underlying etiology for pediatric functional abdominal pain, but intervention with a low-fructose diet is highly successful.

REVIEWER COMMENTS. The approach to evaluate an “adverse food reaction” should be to determine whether it is immune or nonimmune mediated. Although the history for fructose malabsorption will undoubtedly be inconsistent for an IgE-mediated anaphylaxis food reaction, the labeling of a patient with “functional abdominal pain” is equally unsatisfying for the family. Of note, many of the “high-fructose” foods are also the same foods causing oral allergy syndrome, an IgE-mediated process occurring after ingestion of raw fruits that share similar proteins to pollen allergens. Although a fructose BHT may not be readily available, this article provides an excellent fructose food avoidance table that should be considered a valuable resource for both pediatricians and allergists who are evaluating children with adverse food reactions resulting in abdominal pain or underlying chronic functional abdominal pain.

Challenge-Proven Nonsteroidal Anti-Inflammatory Drug Hypersensitivity in Children

PURPOSE OF THE STUDY. The goal of this study was to determine the frequency of true nonsteroidal antiinflammatory drug hypersensitivity (NSAID-H) and whether there were any factors in the history that could predict NSAID-H in children.

STUDY POPULATION. The study population included 58 children, aged 4 months through 17.8 years, with suspected NSAID-H based on a history of acute reactions, including urticaria/angioedema, bronchospasm, laryngeal edema,
Clinical, Serologic, and Histologic Features of Gluten Sensitivity in Children
Matthew F. Feldman and J. Andrew Bird

Pediatrics 2014;134;S157
DOI: 10.1542/peds.2014-1817QQ
Clinical, Serologic, and Histologic Features of Gluten Sensitivity in Children
Matthew F. Feldman and J. Andrew Bird
Pediatrics 2014;134;S157
DOI: 10.1542/peds.2014-1817QQ

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/134/Supplement_3/S157.2.full.html