

The role of intravenous access during oral food challenges in food protein–induced enterocolitis syndrome

Laura E. Pena, M.D.,¹ Danielle Guffey, M.S.,² Charles G. Minard, Ph.D.,² Sara Anvari, M.D.,^{1,3} and Carla M. Davis, M.D.^{1,3}

ABSTRACT

Background: Food protein–induced enterocolitis syndrome (FPIES) is a non–immunoglobulin E mediated food hypersensitivity syndrome characterized by profuse vomiting and diarrhea, which leads to lethargy, dehydration, and hypotension. Given the potential severity of reactions, resolution of FPIES is confirmed via oral food challenge (OFC) during which intravenous (IV) access is recommended to facilitate IV fluids (IVF) and steroid therapy. Risk factors for IV treatment are not well characterized.

Objectives: The objectives of this study were to analyze predictors for IV treatment during OFC in patients with FPIES.

Methods: A retrospective chart review was conducted of patients with The International Classification of Diseases, Ninth Revision codes 558.3 and 558.9, and with OFC who were seen in an allergy and immunology clinic from January 2000 to October 2015. OFC reaction severity was scored (1, mild; 2, moderate; 3, severe), and demographics, IV treatment frequency, and OFC outcomes were evaluated. The Fisher exact test and Wilcoxon rank sum test statistical analyses were performed.

Results: Of 184 patients, 28 met inclusion criteria, with 39 OFCs performed. The median age of onset of FPIES was 6 months. The median age at OFC was 2.6 years. This was 2.2 years (range, 0.3–8.5 years) from symptom onset. Of 39 OFCs, IV treatment, including IVF and/or steroids, was required in only 7.7%. Thirty-eight OFCs (97.4%) were of equal or lesser severity than historical reactions. The median severity of presenting reaction (3[IV+]:1[IV–]; $p = 0.05$) was greater in those who required IV treatment. OFCs with IV treatment were in younger patients (15 months [IV+]:32 months [IV–]; $p = 0.039$) who underwent OFCs earlier relative to the time of diagnosis (8 months [IV+]:28 months [IV–]; $p = 0.018$).

Conclusion: Although FPIES can potentially elicit severe symptomatology, the patients most commonly experienced only vomiting and diarrhea, which often resolved with minimal treatment. Reactions generally did not worsen over time. Fewer than 10% of the patients challenged required IV treatment, all were young and with severe FPIES. It is reasonable to consider age and length of time from historical reactions when evaluating the necessity of IV placement in patients undergoing FPIES OFC.

(Allergy Asthma Proc 38:467–473, 2017; doi: 10.2500/aap.2017.38.4079)

Over the past decade, an increase in food protein–induced hypersensitivity syndrome (FPIES) has been reported, with a recent consensus guideline document that outlines diagnostic criteria.^{1–3} Although FPIES is believed to occur in up to 1 in 300 infants and accounts for 40% of cow's milk intolerance, it is still frequently underrecognized, misdiagnosed, and poorly understood.^{2–5} The recent guidelines state that up to 50% of positive oral food challenge (OFC) results might require treatment with intravenous (IV) fluids.³ FPIES is a non–immunoglobulin E (IgE) mediated food hypersensitivity syndrome believed to be secondary to cell-induced inflammation that results in increased intesti-

nal permeability with increased tumor necrosis factor α in stool samples and decreased T-regulatory cells.^{6–9} Rather than immediate reactions, FPIES is characterized by delayed reactions limited to gastrointestinal manifestations. Patients with FPIES are often young and most commonly present with vomiting and diarrhea 2–10 hours after food ingestion.² Approximately 70% of the reactions are triggered by cow's milk, followed by soybean and grains.¹⁰ Reactions are frequently described as severe and progress to hypotension, with patients appearing seriously ill, with development of shock, dehydration, and hypotension, and require IV fluids (IVF) and hospitalization.¹¹

Given this propensity for severe, life-threatening reactions, conservative management is recommended. Dietary elimination of any FPIES triggers is suggested, and reintroduction of foods at home is not encouraged. FPIES consensus guidelines⁵ state that “some experts strongly recommend that peripheral IV access be secured before OFC.” This has been recommended before challenge for IVF, methylprednisolone, and/or ondansetron administration.⁴ Although the propensity for severe FPIES reactions is widely recognized, many

From the ¹Department of Pediatrics, Baylor College of Medicine, Houston, Texas, ²Dan L Duncan Institute for Clinical and Translational Research, Baylor College of Medicine, Houston, Texas, and ³Department of Allergy and Immunology, Texas Children's Hospital, Houston, Texas

No external funding sources reported

The authors have no conflicts of interest to declare pertaining to this article

Address correspondence to Carla M. Davis, M.D., Department of Allergy and Immunology, Texas Children's Hospital, 6701 Fannin Street, Houston, TX 77030

E-mail address: carlad@bcm.edu

Copyright © 2017, OceanSide Publications, Inc., U.S.A.

parents refuse IV placement before FPIES OFCs despite recommendations. Some physicians do not perform challenges because of the IV recommendation. To our knowledge, no studies to date analyzed the necessity of IV access in FPIES. The objectives of this study were to describe the characteristics of FPIES and OFCs, and to evaluate potential factors that predict IV requirement before FPIES OFC.

METHODS

A retrospective chart review was performed on patients seen from January 1, 2000, to October 3, 2015, with physician-diagnosed FPIES and OFC in the allergy and immunology clinic at a tertiary center. Institutional review board approval was obtained through Baylor College of Medicine (H-23905). Patients were included if they had International Classification of Diseases, Ninth Revision (ICD-9)³ codes 558.3 and 558.9 (allergic/noninfectious gastroenteritis and colitis) and a Current Procedural Terminology (American Medical Association, Chicago, IL) code for food challenge (95076). Patients were excluded if they did not have the ICD-9 code diagnosis or a clinical FPIES diagnosis, or were not given an OFC with the following protocol. FPIES OFC was performed with three equal portions of food protein (0.06–0.6 g/kg) administered over 45 minutes, followed by physician-supervised observation for 3 hours. A positive challenge result was defined as symptoms of emesis, lethargy, or diarrhea, and treatment was administered at the physician's discretion.

Patient demographics, reaction characteristics, IV treatment frequency, and OFC outcomes data were collected. Reaction severity was graded on an internally developed Likert scale (1, mild; 2, moderate; 3, severe). Mild FPIES was defined as either vomiting or diarrhea. Moderate FPIES was defined as having both vomiting and diarrhea. Severe FPIES included any patient with lethargy, dehydration, or clinically significant hypotension. Comparisons of OFC and patient characteristics were made between the patients with positive and negative OFC reactions and between patients who received IV treatment versus no IV treatment. IV treatment was initiated per the treating physician's clinical judgment. Statistical analyses were performed by using the Fisher exact test for comparison of categorical characteristics and the Wilcoxon rank sum test for continuous characteristics. Statistical significance was defined as $p < 0.05$. For analysis, it was assumed that each OFC was independent; however, there were repeated OFCs among six patients. Generalized estimating equations models were used to conduct clustered analyses, but the results were not substantially different from the models when assuming independent observations.

RESULTS

One-hundred and eighty-four patient charts that contained diagnosis codes that pertain to allergic/non-infectious gastroenteritis and colitis (558.3 and 558.9, respectively) or a Current Procedural Terminology code for food challenge (95076) were reviewed. One-hundred and fifty-six patients lacked a diagnosis of FPIES or had no documented OFC and, therefore, were excluded. Twenty-eight patients met inclusion criteria, six of whom underwent more than one OFC to different triggers. Thirty-nine OFCs were performed in 28 patients. The majority of the OFCs were performed in patients who experienced early onset FPIES, with their first reaction having occurred at <9 months of age, with a median age at diagnosis of 6 months (range, 2 days to 46 months). The median number of food triggers ranged from one to six foods, with 16 OFCs in patients who had two or more triggers (Table 1). Sixty-eight percent of OFCs were in patients with reactions to cow's milk, followed by rice (36%), and soy (32%) (Fig. 1).

Most OFC reactions consisted of vomiting (67%) and diarrhea (56%), and no OFCs were performed on a patient with a history of hypotension associated with his or her reactions (Fig. 2). The median severity of both the initial presenting reaction and the last documented reaction before OFC was mild (Table 1). The OFCs were performed by using the FPIES protocol in patients with minimally positive skin-prick test results or serum-specific IgE when the clinical presentation was classic for FPIES and IgE-mediated allergy was not suspected. The number of patients with minimally positive IgE test results >0.35 kU/L was not different in the positive result and the negative OFC result groups. Thirty-five OFCs were performed in patients who had two or more documented reactions after incidental exposures to a single food trigger, whereas only one OFC (2.9%) was associated with a patient who had a worsening severity of symptoms after food ingestion over time.

A strong history of atopy (defined as asthma, allergic rhinitis, or atopic dermatitis) was evident in the majority of patients, and more than half reported a family history of atopy (Table 1). In addition to FPIES, more than one-third of the patients also reported a history of classic IgE-mediated food allergies to alternate foods. Given a high clinical suspicion for FPIES, 30 OFCs were performed in patients who had IgE-specific testing for the offending food agent, and 20% were found to have atypical, IgE positive, FPIES. Only 4% of 26 skin test results were positive. A family history of atopy was associated with no IV treatment for OFC (Table 2).

Of 39 OFCs performed, 13 results were positive. Of those, 10 patients were characterized by either having no treatment or treatment with oral medications, in-

Table 1 Baseline characteristics of patients with FPIES: OFC

FPIES Characteristics	No. of Patients	All Challenges, N = 39	Negative OFC Result, n = 26 (67%)	Positive OFC Result, n = 13 (33%)	p Value
Age at diagnosis, median (25th, 75th percentiles), mo	39	6 (1.5, 12)	3.25 (1.5, 12)	9 (4, 13)	0.28
No. triggers, median (25th, 75th percentiles)	39	2 (1, 3)	2 (1, 3)	2 (1, 3)	0.64
Reaction severity at initial presentation, median (25th, 75th percentiles)	39	1 (1, 2)	1 (1, 2)	1 (1, 1)	0.39
Severity at the final oral food challenge by history, median (25th, 75th percentiles)	35	1 (1, 1)	1 (1, 1)	1 (1, 1)	0.46
Positive IgE result, no. (%)	30	6 (20)	4 (20)	2 (20)	>0.999
Positive skin test result, no. (%)	26	1 (4)	0	1 (10)	0.39
Patient characteristics	28				
Atopy		20 (71)	11 (65)	9 (82)	0.42
Family history atopy		16 (57)	12 (71)	4 (36)	0.12
Food allergies		11 (39)	6 (35)	5 (45)	0.70

FPIES = Food protein–induced enterocolitis syndrome; OFC = oral food challenge; IgE = immunoglobulin E.

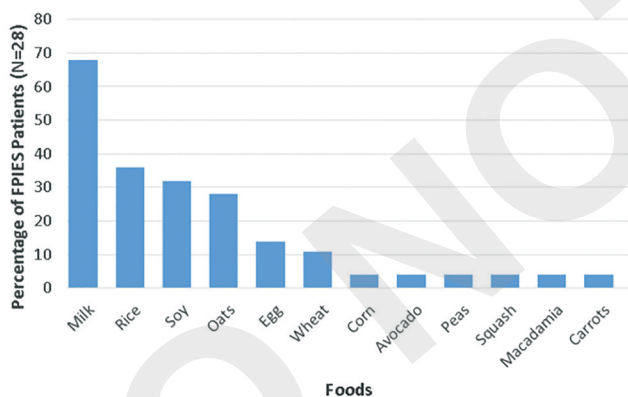


Figure 1. Food triggers for patients with food protein–induced enterocolitis syndrome (FPIES) on initial presentation.

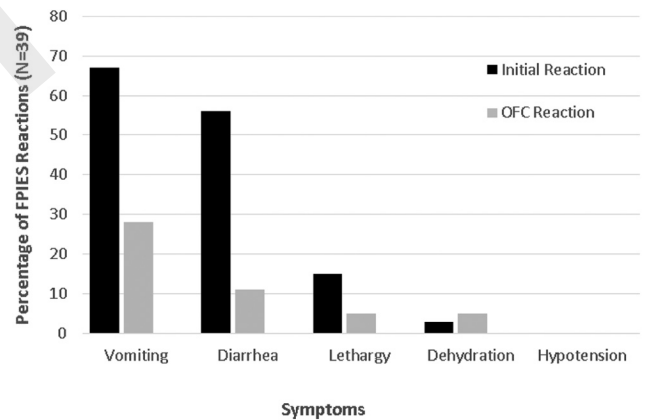


Figure 2. Symptoms of patients with food protein–induced enterocolitis syndrome (FPIES) on initial presentation and with subsequent oral food challenge (OFC).

cluding diphenhydramine, ondansetron, and/or oral rehydration. Three patients who had OFCs required treatment with IVFs and/or IV steroids (Fig. 3). The median age of the patients at OFC was 31 months, which was 27 months from the age of the initial FPIES reaction (Table 3). Eight-five percent of OFC reactions consisted of vomiting, and no OFCs resulted in clinically significant hypotension (Fig. 2). Only one OFC (2.6%) resulted in a reaction of greater severity than historical patient reactions. No patients required hospitalization after completion of OFC. Of the OFCs that documented FPIES resolution ($n = 31$), the median patient age at resolution was 32 months (Table 3). A positive OFC result was associated with later resolution of FPIES (based on documented self-resolution found *via* chart review or proven resolution on subse-

quent OFC) compared with negative OFC results ($p = 0.04$) (Table 3). No statistically significant differences were observed in terms of patient age, number of triggers, presence of atopy, or severity of historical reactions between positive versus negative OFC results (Tables 1 and 3).

In OFCs that required IV treatment, there was only a trend toward more patients having a history of a more-severe initial reaction severity score (SS) (SS = 3) compared with those who did not require IV treatment (SS = 1) ($p = 0.05$) (Table 2). However, this did not meet statistical significance. When severity was analyzed as a potential predictor of OFC outcome, OFCs in patients with an initial severe reaction only trended toward being more likely to result in IV treatment

Table 2 Comparison of baseline patient characteristics and OFC characteristics based on the need for IVT

OFC Characteristics	No. of Patients	No IVT Needed, <i>n</i> = 36 (92%)	IVT Needed, <i>n</i> = 3 (8%)	<i>p</i> Value
Age diagnosis, median (25th, 75th percentiles), mo	39	5.5 (1.25, 12.5)	7 (4, 10)	0.67
No. triggers, median (25th, 75th percentiles)	39	2 (1, 3)	1 (1, 2)	0.11
Reaction severity at the initial presentation, median (25th, 75th percentiles)	39	1 (1, 1)	3 (1, 3)	0.05
Reaction severity at the most recent historical reaction, median (25th, 75th percentiles)	35	1 (1, 1)	1.5 (1, 2)	0.16
IgE positive result, no. (%)	30	6 (21)	0	—
Skin test positive result, no. (%)	26	1 (4)	0	—
Age at OFC, median (25th, 75th percentiles), mo	39	32 (24, 48.5)	15 (8, 30)	0.04
Time to OFC, median (25th, 75th percentiles), mo	39	28 (20, 43)	8 (4, 20)	0.02
Severity of in-office OFC Reaction, median (25th, 75th percentiles)	39	0 (0, 1)	3 (1, 3)	0.002
Hospitalization, no. (%)	39	0	0	—
Age at resolution, median (25th, 75th percentiles), mo	31	32 (24, 44)	36	0.69
Patient characteristics, no. (%)				
Atopy	28	18 (72)	2 (67)	>0.999
Family history of atopy	28	16 (64)	0	0.07
Food allergies	28	10 (40)	1 (33)	>0.999

OFC = Oral food challenge; IVT = intravenous treatment; IgE = immunoglobulin E.

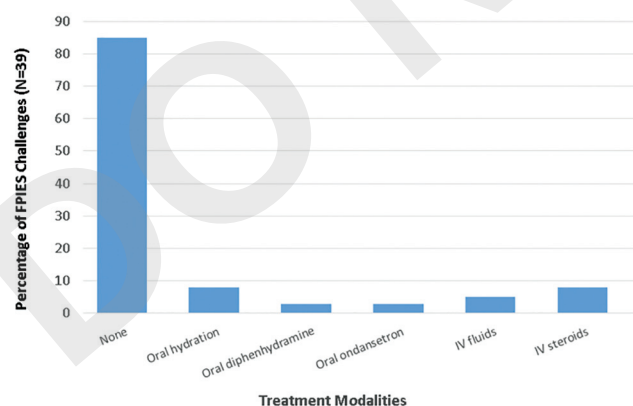


Figure 3. Treatment given to patients with food protein-induced enterocolitis syndrome (FPIES) on oral food challenge in the outpatient clinic.

compared with OFCs in those with mild-moderate reactions ($p = 0.056$) (Table 4). OFCs that resulted in IV treatment were in significantly younger patients than the OFCs without an IV treatment requirement ($p = 0.04$) (Table 2). OFCs in patients <18 months old at the time of challenge had a significantly higher likelihood

of requiring IV treatment compared with OFCs in older patients ($p = 0.01$) (Table 4). In addition, OFC was performed significantly sooner from the time of diagnosis in patients who required IV treatment ($p = 0.02$), and if OFC was performed <12 months from initial presentation, then the risk for IV requirement was significantly increased ($p = 0.004$) (Tables 2 and 4).

DISCUSSION

Over recent years, FPIES has become a widely regarded food hypersensitivity syndrome,³ but the underlying pathogenesis and optimal treatment have not yet been well defined. Reports that describe potentially severe FPIES reactions led to recommendations for IV access for patients undergoing FPIES OFC.^{2,10–16} In 2011, however, Katz *et al.*² first questioned this recommendation on finding that, of 24 OFCs performed, none required IV treatment or had clinically significant hypotension. This study was biased toward a lower acuity of disease, however, because it excluded patients with a history of severe FPIES from undergoing OFCs.² In contrast, the current study analyzed FPIES OFC outcomes among all severities of disease in an

Table 3 Characteristics of patients with FPIES at the time of OFC

	No. of Patients	All Challenges, N = 39	Negative OFC Result, n = 26 (67%)	Positive OFC Result, n = 13 (33%)	p Value
Age at OFC, median (25th, 75th percentiles), mo	39	31 (23, 48)	31.5 (24, 38)	30 (22, 82)	0.52
Time to OFC, median (25th, 75th percentiles), mo	39	27 (19, 43)	24.3 (20, 33.5)	29 (15.5, 56)	0.47
Severity score for reaction, median (25th, 75th percentiles)	39	0 (0, 1)	0 (0, 0)	1 (1, 1)	<0.001
Hospitalization, no. (%)	39	0	0	0	—
Age at resolution, median (25th, 75th percentiles), mo	31	32 (24, 44)	31.5 (24, 38)	39 (36, 61)	0.04

FPIES = Food protein–induced enterocolitis syndrome; OFC = oral food challenge.

Table 4 Predictive indicators for an IVT requirement during OFC

	All Challenges, N = 39	No IVT Needed, n = 36 (92%)	IVT Needed, n = 3 (8%)	p Value
Severity at first reaction				0.06
Mild-moderate (SS 1, 2)	33	32	1	
Severe (SS, 3)	6	4	2	
Age at OFC				0.01
<18 mo	3	1	2	
≥18 mo	36	35	1	
Time to OFC				0.004
<12 mo	2	0	2	
≥12 mo	37	36	1	

IVT = Intravenous treatment; OFC = oral food challenge; SS = severity scale.

outpatient setting and highlighted findings that challenge the current guidelines.

Based on the patient characteristics described, this study population represented the FPIES population as a whole. This study confirmed that patients with FPIES were mostly infants who presented within the first 6 months of life with vomiting and diarrhea, typically secondary to a cow's milk trigger.^{10–16} Although the majority of studies found soy to be the second most common trigger and rice to be the most common solid food FPIES trigger, our study found rice to cause 36% of FPIES, followed by soy, which caused 32% of FPIES (Fig. 1). The slightly decreased prevalence of soy FPIES in this population compared with the literature may be due to frequent early introduction of rice cereal, with a lower and later exposure to soy milk. Patients with an allergy or FPIES reaction to cow's milk may have been discouraged from introducing soy due to a reported 50% cross-reactivity as well as a common parental fear of a detrimental effect of estrogen content in soy formula on a child's development.^{17,18}

In addition, the results of this study supported earlier accounts in the literature of patients with FPIES who commonly (57% in our study) developed multiple FPIES food triggers.^{5,10,11,13–16} The presence of atopy (allergic rhinitis, asthma, atopic dermatitis) is a well-known association with FPIES that was also mimicked in this study. Almost three-fourths of this FPIES patient population had atopic disease and 57% reported a family history of atopy, which was consistent with previous studies that describe concomitant atopy as high as 30%, and 20–80% with a family history of atopic disease.^{11,13,19,20}

Although the characteristics of the FPIES population in this cohort seemed to coincide with that described in the literature, the results did not reflect the severity of reactions previously reported. Other studies found that 75% of patients with FPIES seem acutely ill and that 15% require hospitalization for hypotension.⁴ In solid food FPIES, 79% of patients present with severe reactions, 57% of whom seem in shock, and 64% require hospitalization.¹¹ In contrast, 0% of our patients dem-

onstrated clinically significant hypotension, and none were hospitalized. In addition, this study did not demonstrate a worsening severity of reactions over time. Concern for interval worsening of FPIES reactions arose from Bansal *et al.*²¹ and Monti *et al.*,²² who described increased sensitivity on subsequent exposures to the same food antigen. However, only 1 of 39 OFCs in this study resulted in a reaction more severe than historical reactions, which thus alleviated the concern that an OFC may produce an unexpectedly severe reaction.

IV treatment has been a mainstay of therapy for acute FPIES reactions. Only three challenges (7.7%) in our study elicited a reaction that warranted treatment with IVF and/or IV steroids. Three additional positive OFC reactions resolved with oral rehydration and/or oral medications alone, whereas the remaining seven positive OFC results required no intervention. Generally, the patients who required no treatment involved those with substantially delayed reactions that occurred at home after the period of physician observation. Reactions were not severe enough to warrant seeking medical attention, and symptoms, typically recurrent emesis, self-resolved.

Although establishing IV access in every FPIES OFC may not be essential, certain considerations should be made in high-risk situations. The patients who presented for OFC at a young age, with minimal time elapsed since the initial reaction, were significantly more likely to experience a reaction that required IV treatment. Results of a recent study from Korea indicated sooner challenges may be permissible but continued to endorse waiting until at least 12 months of age to perform cow's milk FPIES challenge.²³ If electing to perform OFC sooner than 12 months after previous reactions, obtaining IV access is prudent. Allergists may have difficulty implementing OFCs for FPIES because of the perceived need for IV placement. Young children may need many personnel to restrain them for IV placement. Frequently, this is traumatic for the family. In addition, office workflow issues and parental refusal of oral challenge may arise due to the invasive procedure. The quality of life would likely be enhanced in patients who have this diagnostic procedure,²⁴ so there is potential benefit to stratifying risk for OFCs in patients with FPIES and with the features that correspond to milder reactions (older age, longer length of time from historical reactions). This would enable allergists to make more accurate diagnoses of FPIES and eliminate FPIES as a cause of emesis in patients with mild symptoms or questionable histories.

Due to the retrospective nature, our study was limited by the information supplied in the electronic medical record. FPIES is a clinical diagnosis, which thus relied on clinicians' ability to detect and document the disease. Also, ICD-9 codes were screened to obtain

patients who met inclusion criteria, and, because no one ICD-9 code for FPIES existed in the past, some patients with FPIES were likely overlooked. This study only encompassed patients who presented and were seen in the allergy and immunology clinic, and who were compliant to follow-up for OFC. The change in OFC frequency over time was not assessed due to the small number of patients. However, there were no efforts to change the management of FPIES with regard to OFCs during the time frame studied. Other patients with FPIES may not have been incorporated into this study if they were seen in the emergency department, never referred, or lost to follow-up. It is feasible that the reaction severity of patients in the study might have underrepresented those with severe FPIES if the patients with severe reactions were underrecognized and misdiagnosed as sepsis, for example. Lastly, given the very small percentage of patients who required IV treatment for a FPIES OFC reaction, significance was difficult to determine in many cases, and future prospective studies are necessary to confirm the predictive factors reported.

To our knowledge, this was the first study to date to describe patients with FPIES OFCs in an outpatient setting, assessed the need for IV access during an FPIES OFC, and, more precisely, determined criteria that delineated the necessity of IV placement. This study incorporated a large sample size collected over a 15-year span. The patients presented to the outpatient clinic and, therefore, are thought to adequately represent the pediatric FPIES outpatient population as a whole. This study also characterized FPIES reactions over time and analyzed the risk for interval worsening of reactions.

CONCLUSION

FPIES is a clinical syndrome, which typically manifests as vomiting and diarrhea. Ninety-seven percent of OFCs result in similar or milder reactions on subsequent exposures to offending food antigens in this population, and, although universal IV placement during FPIES OFC has been recommended, >90% of these IVs may be placed unnecessarily. Special consideration should be given to infants <18 months old and those who presented for OFC despite a recent reaction because these patients were significantly more likely to require IV treatment after OFC.

REFERENCES

1. Arik Yilmaz E, Soyer O, Cavkaytar O, et al. Characteristics of children with food protein-induced enterocolitis and allergic proctocolitis. *Allergy Asthma Proc* 38:54–62, 2017.
2. Katz Y, Goldberg MR, Rajuan N, et al. The prevalence and natural course of food protein-induced enterocolitis syndrome to cow's milk: A large-scale, prospective population-based study. *J Allergy Clin Immunol* 127:647–653.e1–3, 2011.

3. Nowak-Węgrzyn A, Chehade M, Groetch ME, 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* 139:1111–1126.e4, 2017.
4. Nowak-Węgrzyn A. Food protein-induced enterocolitis syndrome and allergic proctocolitis. *Allergy Asthma Proc* 36:172–184, 2015.
5. Nowak-Węgrzyn A, Katz Y, Mehr SS, and Koletzko S. Non-IgE-mediated gastrointestinal food allergy. *J Allergy Clin Immunol* 135:1114–1124, 2015.
6. Heyman M, Darmon N, Dupont C, et al. Mononuclear cells from infants allergic to cow's milk secrete tumor necrosis factor alpha, altering intestinal function. *Gastroenterology* 106:1514–1523, 1994.
7. Kapel N, Matarazzo P, Haouchine D, et al. Fecal tumor necrosis factor, eosinophil cationic protein and IgE levels in infants with cow's milk allergy and gastrointestinal manifestations. *Clin Chem Lab Med* 37:29–32, 1999.
8. Chung HL, Hwang JB, Park JJ, and Kim SG. Expression of transforming growth factor beta, transforming growth factor type I and II receptors, and TNF-alpha in the mucosa of the small intestine in infants with food protein-induced enterocolitis syndrome. *J Allergy Clin Immunol* 109:150–154, 2002.
9. Karlsson MR, Rugtveit J, and Brandtzaeg P. Allergen-responsive CD4+ CD25+ regulatory T cells in children who have outgrown cow's milk allergy. *J Exp Med* 199:1679–1688, 2004.
10. Ruffner MA, Ruymann K, Barni S, et al. Food protein-induced enterocolitis syndrome: Insights from review of a large referral population. *J Allergy Clin Immunol Pract* 1:343–349, 2013.
11. Nowak-Węgrzyn A, Sampson HA, Wood RA, and Sicherer SH. Food protein-induced enterocolitis syndrome caused by solid food proteins. *Pediatrics* 111:829–835, 2003.
12. Mehr SS, Kakakios AM, and Kemp AS. Rice: A common and severe cause of food protein-induced enterocolitis syndrome. *Arch Dis Child* 94:220–223, 2009.
13. Sicherer SH, Eigenmann PA, and Sampson HA. Clinical features of food protein-induced enterocolitis syndrome. *J Pediatr* 133:214–219, 1998.
14. Jarvinen-Seppo KM, Sickles L, and Nowak-Węgrzyn AH. Clinical characteristics of children with food protein-induced enterocolitis (FPIES). *J Allergy Clin Immunol* 125 (suppl. 1):AB85, 2010(Abs).
15. Fogg MI, Brown-Whitehorn TA, Pawlowski NA, and Spergel JM. Atopy patch test for the diagnosis of food protein-induced enterocolitis syndrome. *Pediatr Allergy Immunol* 17:351–355, 2006.
16. Mehr S, Kakakios A, Frith K, and Kemp AS. Food protein-induced enterocolitis syndrome: 16-year experience. *Pediatrics* 123:e459–e464, 2009.
17. McDonald PJ, Goldblum RM, Van Sickle GJ, and Powell GK. Food protein-induced enterocolitis: Altered antibody response to ingested antigen. *Pediatr Res* 18:751–755, 1984.
18. Burks AW, Casteel HB, Fiedorek SC, et al. Prospective oral food challenge study of two soybean protein isolates in patients with possible milk or soy protein enterocolitis. *Pediatr Allergy Immunol* 5:40–45, 1994.
19. Mehr S, Frith K, Barnes EH, et al. Food protein-induced enterocolitis syndrome in Australia: A population-based study, 2012–2014. *J Allergy Clin Immunol*, 2017. (Epub ahead of print April 18, 2017.)
20. Gryboski JD. Gastrointestinal milk allergy in infants. *Pediatrics* 40:354–362, 1967.
21. Bansal AS, Bhaskaran S, and Bansal RA. Four infants presenting with severe vomiting in solid food-protein induced enterocolitis syndrome: A case series. *J Med Case Rep* 6:160–164, 2012.
22. Monti G, Castagno E, Liguori SA, et al. Food protein-induced enterocolitis syndrome by cow's milk proteins passed through breast milk. *J Allergy Clin Immunol* 127:679–680, 2011.
23. Hwang JB, Sohn SM, and Kim AS. Prospective follow-up oral food challenge in food protein-induced enterocolitis syndrome. *Arch Dis Child* 94:425–428, 2009.
24. Franxman TJ, Howe L, Teich E, and Greenhawt MJ. Oral food challenge and food allergy quality of life in caregivers of children with food allergy. *J Allergy Clin Immunol Pract* 3:50–56, 2015. □

Copyright of Allergy & Asthma Proceedings is the property of OceanSide Publications Inc. and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.