BRIEF REPORT

WILEY

Adherence to dietary prescriptions in patients with acute food protein-induced enterocolitis syndrome

Stefano Miceli Sopo[1] | Dario Sinatti[2] | Giorgio Sodero[2] | Mariannita Gelsomino[2] | Francesco Mastellone[2]

[1]Department of Life Sciences and Public Health, Pediatric Allergy Unit, Pediatrics Section, Policlinico Gemelli Universitary Foundation IRCCS, Catholic University of Sacre Hearth, Rome, Italy
[2]Department of Life Sciences and Public Health, Post-Graduate School of Pediatrics, Policlinico Gemelli Universitary Foundation IRCCS, Catholic University of Sacre Hearth, Rome, Italy

Correspondence
Dario Sinatti, Department of Life Sciences and Public Health, Pediatric Allergy Unit, Pediatrics Section, Policlinico Gemelli Universitary Foundation IRCCS, Catholic University of Sacre Hearth, Rome 00168, Italy.
Email: dsinatti@gmail.com

Received: 21 January 2022
Accepted: 17 May 2022

ABSTRACT

Food protein-induced enterocolitis syndrome (FPIES) is a non-Immunoglobulin (non-IgE)-mediated food allergy. The elimination diet is the only therapy, the culprit food will be reintroduced if tolerance is acquired. However, it is possible that patients do not follow the recommendations given by the healthcare professional. We investigated if our advice to avoid the trigger food in patients with active FPIES and to reintroduce it in the diet in patients who achieved tolerance had been implemented. We interviewed by telephone the parents of children who were diagnosed with acute FPIES. About 23.2% of our patients disregarded our dietary recommendations: 6/42 (14.3%) of patients who passed a tolerance oral food challenge (OFC) did not eat the trigger food, 4/22 (18.2%) of patients who failed OFC ate the trigger food, and 9/18 (50.0%) of patients who did not perform a tolerance OFC ate the trigger food. We have analyzed some possible influencing factors and no difference was found to be statistically significant. Our results are in line with those reported for IgE-mediated food allergies. As has already been proposed by others, we suggest reassessing food consumption in all patients after a food challenge.

KEYWORDS

Adherence, Dietary management, Follow up, Food protein-induced enterocolitis syndrome

INTRODUCTION

Food protein-induced enterocolitis syndrome (FPIES) is a non-Immunoglobulin E (non-IgE)-mediated food allergy (FA) characterized by repetitive, often projectile, vomiting within 1–4 h of food ingestion, that may be associated with lethargy and pallor.[1] Appropriate dietary management implies supporting normal growth and development, avoidance of allergens, and advancement of complementary foods.[2] The key to successfully eliminating trigger food is avoidance to prevent reactions without excessive avoidance that may interfere with food choices and

DOI: 10.1002/ped4.12333

nutritional intake.[2] However, it is possible that patients and their families do not follow the recommendations given by the healthcare professional. Patients with multiple triggers, for example, are more likely to develop food aversion.[3] Moreover, prophylactic multiple food avoidance may be more common.[2] About 70% of caregivers reported that their children avoided at least two food groups because of FPIES.[4] We wanted to verify the adherence of our dietetic prescriptions in our outpatients diagnosed with acute FPIES in the last 15 years.

METHODS

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the issued Policlinico Gemelli Universitary Foundation Ethics Committee, the code of the event report is Prot. ID 3920. Written informed consent was obtained from the children's parents for all procedures performed.

Interviewing

We interviewed by telephone the parents of children, consecutively referred from September 2005 to July 2021 to the allergy unit of Policlinico Gemelli Universitary Foundation, who was diagnosed with acute FPIES. The anamnestic diagnosis of acute FPIES was made if patients fulfilled the criteria of Miceli Sopo et al.[5] Children underwent diagnostic oral food challenge (OFC) if the FPIES criteria were not met or to verify the acquisition of tolerance after 12–18 months from the last acute FPIES episode.[5] OFC was almost always performed administrating a single dose of incriminated food, in quantities at least equal to a full serving size for age, followed by 4 hours of observation.[6] The skin prick tests were performed at the time of diagnosis to detect classic or atypical FPIES and just before the OFC. The interviews were conducted using a specific questionnaire that is available on request to the corresponding author. The questionnaire investigated if the patient ingested and appreciated the trigger food (and contiguous foods, such as beef for cow's milk). In children with multiple FPIES, the investigation was referred to the first (in order of time) trigger food involved.

Analysis

Also, we have analyzed some possible influencing factors: a) the time elapsed since the last contact with us (if greater or less than 2 years); b) the age of the patient at the time of the last contact with us (whether older or younger than 2 years); c) the presence or absence of atopy markers; d) the type of trigger food (whether cow's milk or other). Data were entered into an Excel spreadsheet 2020. The statistical analysis used the Statistics for Biomedical disciplines program (from the Primer of Biostatistics by Stanton Glantz, 6th edition (McGraw Hill)). Continuous data were described as the mean (standard deviation) and as frequencies/percentages for categorical variables. Comparisons between the groups were evaluated using Fisher's exact test or the chi-square test. We used a 2×2 table to calculate the negative predictive value (NPV). A value $P < 0.05$ was considered significant.

RESULTS

The parents of 82 patients were interviewed. Parents of another 10 patients refused to be interviewed ($n = 3$) or were unavailable ($n = 7$). The interviews were made on average about 57 ± 43 months after the last medical visit with the patient and his family (range 1.6–188 months). In almost all cases, two phone calls were made and the second one was to clarify some details. The main characteristics of the patients enrolled are shown in Table 1. The age at diagnosis was 25 ± 30 months (range 3–140 months) and the age at follow-up was 94 ± 49 months (range 12–217 months).

Table 2 shows the main results. About 23.2% of our patients disregarded our dietary recommendations: 6/42 (14.3%) of patients who passed a tolerance OFC did not eat the trigger food, 4/22 (18.2%) of patients who failed OFC ate the trigger food, and 9/18 (50.0%) of patients who did not perform a tolerance OFC ate the trigger food.

Overall, at the time of the interview 49/82 (59.8%) of our patients ate the trigger food. Most of the children who passed an OFC ate the trigger food (36/42, 85.7%), but even among children whose parents did not perform an OFC tolerance, this percentage was high (9/18, 50.0%). Most of the patients who ate the trigger food did not do it properly (32/49, 65.3%): for instance, they ate parmesan cheese but did not drink cow's milk, or ate the chicken's egg only inside bakery products, or only one type of fish.

Nineteen patients ate the trigger food just because they were allowed to eat meals prepared with that food, 14 because they liked it, seven because they felt safer in this way, 6 ate it even though they did not like it, and three patients did not care if they could eat or not the trigger food.

Of the eight patients with cow's milk FPIES who did not eat the trigger food, none ingested the milk of other mammals, seven ate beef and seven ate commercial products that could contain traces of cow's milk. Of the 10 patients with fish FPIES who did not eat the trigger food, two ate other types of fish, six ate shellfish, and eight ate foods that could contain traces of fish. Of the seven patients with chicken's egg, FPIES did not eat the trigger food, none ingested other

TABLE 1 Demographic and clinical characteristics of participants with food protein-induced enterocolitis syndrome (FPIES)

Variables	Number of patients, *n* (%)
Male	39 (47.6)
Age at diagnosis (months)	3–140
Age at follow up (months)	12–217
Anamnestic diagnosis	52 (63.4)
OFC diagnosis	30 (36.6)
Atypical FPIES	6 (7.3)
Multiple FPIES	7 (8.5)
OFC for tolerance passed	42 (51.2)
OFC for tolerance failed	22 (26.8)
OFC for tolerance not performed	18 (22.0)
Trigger food	
Cow's milk	42 (51.2)
Fish	16 (19.5)
Chicken's egg	11 (13.4)
Grains	7 (8.6)
Shellfish	2 (2.4)
Chicken's meat	2 (2.4)
Fruit	2 (2.4)
Atopic comorbidities	
Atopic dermatitis	16 (19.5)
Asthma	3 (3.6)
Allergic rhinitis	7 (8.5)
IgE-mediated food allergies	2 (2.4)
Drug allergies	2 (2.4)
Gastrointestinal diseases	
Gastroesophageal reflux disease	3 (3.6)
Recurrent abdominal pain	5 (6.1)
Constipation	2 (2.4)

Data are presented as *n* (%) or range. FPIES, food protein-induced enterocolitis syndrome; OFC, oral food challenge.

types of eggs, five ate poultry meat, and six ate foods that could contain traces of egg. Of the two patients with rice, FPIES did not eat the trigger food, both ate other grains, and none ate foods that could contain traces of rice.

Of the 6/42 (14.3%) patients with passed OFC with what was their trigger food and then did not eat that food despite our recommendation to do so, four did not eat it because they did not like it, and two did not eat it because they had presented an adverse reaction after the reintroduction at home. One of the last two children had received the diagnosis of tolerance even though he had only eaten 30% of a normal dose (according to age) of the trigger food (cod) because he refused to continue the OFC; he subsequently ate at home a normal portion and had a typical adverse reaction. Of the 4/22 (18.2%) patients with failed OFC who ate the trigger food, all had started, at least 2 years after the last failed OFC, to ingest small quantities of the cooked trigger food at home. In two patients the trigger food was cow's milk, in the other two patients the chicken's egg.

Of the 18/22 (81.8%) patients with failed OFC who did not eat the trigger food, eight had no longer performed other reintroduction attempts, and 10 had tried to reintegrate at home, which failed for eight patients and passed for two (who, however, do not eat the trigger food out of dislike). Of the 9/18 (50.0%) patients with OFC not performed who ate the trigger food, three ate it only partially. Of the nine patients with OFC not performed who did not eat the trigger food, seven reported not having done so in compliance with the dietary prescriptions we provided, two decided to reintegrate the trigger food at home causing a typical allergic reaction (one patient), or aversion (one patient).

Regardless of the type of trigger food, there were no differences in acceptance by the child or by the parents, the introduction of different foods considered "distant" from the trigger one before and after the onset of FPIES. None of the comparisons regarding possible influencing factors resulted in a statistically significant difference.

TABLE 2 Ingestion or not of the trigger food according to the results of the oral food challenge (OFC)

	Passed OFC			Failed OFC			OFC not performed		
Trigger food	Eats freely	Eats partially	Does not eat	Eats freely	Eats partially	Does not eat	Eats freely	Eats partially	Does not eat
All together	13	23	6	1	3	18	3	6	9
Cow's milk	10	18	2	0	2	6	2	2	0
Fish	0	1	2	0	0	6	1	4	2
Chicken's egg	1	1	2	1	1	3	0	0	2
Grains	2	3	0	0	0	2	0	0	0

OFC, oral food challenge.

DISCUSSION

Almost 1/4 of our patients did not follow our dietary indications. This problem has already been pointed out in the literature about food allergies. Eigenmann et al.[7] reported that 1/4 of previously allergic patients continue a food avoidance diet despite a negative OFC. Flammarion et al.[8] also reported that after an OFC passed, two families never proposed the food (lentil and tomato) for fear of allergic reaction and three children refused to eat it (almond, peanut, and egg). We reported[9] that in 8% of cases food was not given at all and parents' motivations were: fear of an adverse reaction, doubts regarding the persistence of allergy, and different advice from a general practitioner or another allergist, and children lack preference. Moreover, we noticed that children >2-year-old introduced to tested food less frequently than infants.

Regarding FPIES, food aversion[3] and prophylactic multiple food avoidance[2] have been reported. Maciag et al.[4] described that, in their cohort, many who avoided both rice and oat also avoided wheat (56/116). It is not known how many children reacted to wheat versus empirically avoided it after reacting to other grains. The authors conclude that while some of these foods may be emerging triggers of FPIES, it is also possible that concern for FPIES in a highly aware caregiver may be associated with overavoidance of certain foods that are not actual triggers of FPIES.[4]

We believe that one of the reasons for these behaviors could be the lack of active and short-term follow-up for patients after an OFC. In our daily clinical practice, we suggest reintroducing the food to the patient's diet, but we do not schedule a new appointment to verify if the suggestion has been followed. The lack of a recall of patients who do not show up for a first OFC, or for another OFC after having failed one, also was associated with determining these results. We schedule an appointment, but if the patient does not show up, we do not contact him again to propose another one. Therefore, our management of patients with acute FPIES has been modified and the two deficiencies described above have been eliminated. Obviously, this requires more commitment in terms of human and economic resources. It is also not guaranteed that the desired management improvement can be achieved and preserved always and everywhere.

In this study, we have established that the problem of adherence to recommendations also exists for patients with acute FPIES, and in a substantial percentage. We propose to carry out a future study to evaluate possible psychosocial components, language barriers, and any other difficulties in implementing the recommendations we make to patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. 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;139:1111-1126. DOI: 10.1016/j.jaci.2016.12.966
2. Groetch M, Baker MG, Durban R, Meyer R, Venter C, Muraro A. The practical dietary management of food protein-induced enterocolitis syndrome. *Ann Allergy Asthma Immunol.* 2021;127:28-35. DOI: 10.1016/j.anai.2021.03.007
3. Su KW, Patil SU, Stockbridge JL, Martin VM, Virkud YV, Huang JL, et al. Food aversion and poor weight gain in food protein-induced enterocolitis syndrome: a retrospective study. *J Allergy Clin Immunol.* 2020;145:1430-1437. DOI: 10.1016/j.jaci.2020.01.001
4. Maciag MC, Bartnikas LM, Sicherer SH, Herbert LJ, Young MC, Matney F, et al. A slice of food protein-induced enterocolitis syndrome (FPIES): insights from 441 children with FPIES as provided by caregivers in the international FPIES association. *J Allergy Clin Immunol Pract.* 2020;8:1702-1709. DOI: 10.1016/j.jaip.2020.01.030
5. Miceli Sopo S, Greco M, Monaco S, Tripodi S, Calvani M. Food protein-induced enterocolitis syndrome, from practice to theory. *Expert Rev Clin Immunol.* 2013;9:707-715. DOI: 10.1586/1744666X.2013.814418
6. Miceli Sopo S, Sinatti D, Gelsomino M. Retrospective analysis of 222 oral food challenges with a single dose in acute food protein-induced enterocolitis syndrome. *Pediatr Allergy Immunol.* 2021;32:1066-1072. DOI: 10.1111/pai.13489
7. Eigenmann PA, Caubet JC, Zamora SA. Continuing food-avoidance diets after negative food challenges. *Pediatr Allergy Immunol.* 2006;17:601-605. DOI: 10.1111/j.1399-3038.2006.00455.x
8. Flammarion S, Santos C, Romero D, Thumerelle C, Deschildre A. Changes in diet and life of children with food allergies after a negative food challenge. *Allergy.* 2010;65:797-798. DOI: 10.1111/j.1398-9995.2009.02239.x
9. Miceli Sopo S, Monaco S, Greco M, Onesimo R. Prevalence of adverse reactions following a passed oral food challenge and factors affecting successful re-introduction of foods. A retrospective study of a cohort of 199 children. *Allergol Immunopathol.* 2016;44:54-58. DOI: 10.1016/j.aller.2015.04.010

How to cite this article: Miceli Sopo S, Sinatti D, Sodero G, Gelsomino M, Mastellone F. Adherence to dietary prescriptions in patients with acute food protein-induced enterocolitis syndrome. *Pediatr Investig*. 2022;6:207–210. https://doi.org/10.1002/ped4.12333