



Perspective

CON: Peripheral intravenous access should always be secured before initiating food protein-induced enterocolitis syndrome oral food challenge



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Food protein-induced enterocolitis syndrome (FPIES) is a non-immunoglobulin E-mediated food allergy that can cause severe reactions characterized by delayed-onset vomiting and diarrhea leading to dehydration and possible hypotension and shock. Although these reactions can be severe, many require only supportive care. Because it can be clinically challenging to predict the severity of FPIES reactions, many physicians opt to obtain an intravenous access before performing an oral food challenge (OFC) in patients with FPIES.

In 2017, the international consensus guidelines provided recommendations for the care of patients with FPIES, including the role of OFCs for diagnostic purposes and to assess for FPIES resolution. However, there continues to be considerable practice variability regarding how OFCs are conducted and the protocols that are used. The 2017 consensus guidelines do not provide specific recommendation whether or not an intravenous line must be placed before proceeding with OFC for FPIES but rather state that up to 50% of those with positive OFC result may require treatment with intravenous fluids and intravenous rehydration, which should be readily available.¹ A foundation for this recommendation was an evidence from the 2014 study by Caubet et al, which is referenced in the guidelines, and described a cohort of 180 patients with FPIES undergoing OFC for FPIES, of whom 41% reacted at the time of challenge.¹ In this series, most patients with a positive challenge result (96%) were treated with intravenous fluids, but given that

some patients reacted, intravenous fluids were used in just 36% of the overall challenges.

Several centers have published case series that detail OFC.^{1–5} The data contained in these publications suggest that intravenous placement may not be necessary for all cases of physician-supervised OFC procedures when following the current guidelines. This is primarily owing to the fact that with the current protocols and referral practices, most patients do not have FPIES reactions during food challenges and only a subset of those patients who do react require intravenous fluids to manage the reactions.

Geographic variations remain an important consideration in FPIES, because the prevalence of reactions to specific food antigens varies by geographic region but does not seem to change the rate of intravenous fluid resuscitation. In the Italian cohort of Barni et al,³ 19 of 54 patients (35%) had FPIES reactions and 11 required intravenous fluids (57% of the reactors and 20% of the total OFC).² Furthermore, in a retrospective review of 81 FPIES OFCs from Spain, 33 patients had a positive challenge result and 19 required intravenous fluids (57% of the reactors and 23% of the total).³ In 2 other non-European or US studies, the authors found infrequent or no use of intravenous fluid administration after FPIES OFC. Katz et al have published cow's milk FPIES OFC results for 28 patients (reviewed in Nowak-Węgrzyn et al¹), in which all patients had reactions, but none needed intravenous fluids. Overall, in the non-US studies, less than 25% of all challenged patients needed intravenous fluids.

More recent studies from the United States report even lower use of intravenous fluid after the reactions. In a series from the Children's Hospital of Philadelphia, of 169 patients undergoing a FPIES OFC, 10% had acute reactions (17 total) and 14 received intravenous fluids (82% of positive challenge results, only 8.3% of

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total challenges).⁴ Guenther et al⁵ recently published data from FPIES OFC with 10 of 88 patients reacting at OFC (11.4%); 90% were managed with some combination of oral, intramuscular, or intravenous ondansetron and only 1 patient required intravenous fluids. There are no other studies with uniform administration of ondansetron following OFC, so it is not clear whether this approach would uniformly decrease the need for intravenous fluid administration following FPIES OFC.

In examining those who might require intravenous access before starting an OFC for FPIES, the current data suggest that 45% to 90% of patients undergoing OFC tolerate the challenged food. Therefore, many patients are likely to progress through OFC without the need for any clinical intervention, because they will ultimately tolerate the challenged food. The clinical conundrum, at present, remains with identifying those patients at risk of a reaction, given that there is no specific testing available for FPIES.

Clinical criteria remain important when recommending FPIES OFC to patients. The average age of tolerance acquisition is variable by the type of triggering food allergen, and these data can be used to help plan OFC timing to minimize risk.¹ Most of these data are retrospective, and therefore, the estimates provided may be conservative. Nonetheless, these time frames can help clinicians provide anticipatory guidance to families to consider when deciding on intravenous placement at the time of challenge. As increasing information becomes available on specific food antigens, it may be possible to offer patients increasingly more specific guidance on the overall risk of reaction and provide rational guidance on how long to wait before performing a challenge to minimize risk.

Our recommendations are that clinicians must be able to establish immediate intravenous access in the event of a severe reaction during the challenge to provide fluids and medications.

Placing an intravenous line before the challenge may not be necessary in all cases because the number of patients who actually need intravenous fluids is low, similar to the combined US and non-US studies in which only 19% of all patients with FPIES undergoing challenge required intravenous fluids. Even if an intravenous access is not obtained at the start of the OFC, patients and families should be advised on the risk of reaction and potential need for intravenous fluids as part of the consent process for FPIES OFC. Additional clinical information including medical or behavioral factors that would either compromise patient safety or complicate intravenous placement within the context of a reaction should be considered and may influence the decision to place an intravenous line before beginning the challenge. In addition, we recommend intravenous placement before FPIES OFC in patients with a history of severe FPIES reactions and in the rare clinical case when a diagnostic FPIES OFC may be necessary.

References

1. Nowak-Węgrzyn A, Berin MC, Mehr S. Food protein-induced enterocolitis syndrome. *J Allergy Clin Immunol Pract*. 2020;8(1):24–35.
2. Wang KY, Lee J, Cianferoni A, et al. Food protein-induced enterocolitis syndrome food challenges: experience from a large referral center. *J Allergy Clin Immunol Pract*. 2019;7(2):444–450.
3. Barni S, Sarti L, Mori F, Liotti L, Pucci N, Novembre E. A modified oral food challenge in children with food protein-induced enterocolitis syndrome. *Clin Exp Allergy*. 2019;49(12):1633–1636.
4. Vazquez-Ortiz M, Machinena A, Dominguez O, et al. Food protein-induced enterocolitis syndrome to fish and egg usually resolves by age 5 years in Spanish children. *J Allergy Clin Immunol Pract*. 2017;5(2):512–515.e1.
5. Guenther MW, Crain M, Parrish CP, Bird JA. An observed serving dose may not be necessary following a standard divided-dose FPIES oral food challenge. *J Allergy Clin Immunol Pract*. 2020;8(4):1462–1464.