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Editorial

Where to challenge?

That is the question

Over the years, questions of why, where, when, and how to perform oral food challenges (OFCs) for food protein-induced enterocolitis syndrome (FPIES) have been asked. Given the lack of diagnostic and prognostic biomarkers, OFC remains the gold standard for confirming FPIES diagnosis and assessing resolution.[1,2]

Heterogeneity exists regarding FPIES OFC dosing, observation time, and setting.[3,4] Traditionally, these OFCs are performed 12 to 18 months after the last symptomatic exposure, in medically supervised settings, using single- or multi-dose protocols, with prolonged observation and recommendation to secure intravenous placement, particularly in patients with previous severe reactions.[3,4]

Sanders et al[5] now ask whether some FPIES OFCs be performed at home—evaluated through a cost-effectiveness lens. To consider the answer, we must evaluate the pros and cons of medically supervised vs at-home FPIES OFCs and the assumptions in the model of Sanders et al.[5]

There are many barriers to carrying out medically supervised FPIES OFCs, which home-based OFCs can overcome. Barriers identified by allergists to OFCs in general include time, space, staffing, experience, hospital proximity, and insurance reimbursement.[6] These barriers are compounded in FPIES OFCs, which are more time intensive and may require intravenous placement, leading to a shortage of allergists equipped and comfortable to perform them. In many cases, the allergist who diagnoses and manages a patient's FPIES may not work in a practice that offers FPIES OFCs, leading to referral to another allergist for OFC, increasing time and cost to families and the health care system, and delaying the OFC.

Families face barriers of access to care and timeliness of medically supervised OFCs, which can be overcome by at-home OFCs. Patients may need to travel long distances to find allergists knowledgeable in FPIES and who offer OFCs, limiting access to care. Patients and families need to take time off school/work and arrange and pay for backup-dependent care to accommodate time-intensive medically supervised OFCs. Owing to resource limitations, many patients face long wait times for OFCs. Medically supervised compared with at-home OFCs are associated with increased time from last reaction to confirmed resolution (median, 25.0 vs 17.1 months).[7] Requiring medical supervision for OFCs may increase anxiety if families perceive that this is an unsafe procedure requiring management in a specialized setting, potentially leading to prolonged, unnecessary, and potentially detrimental food avoidance. Improving access to FPIES OFCs through at-home OFCs to guide dietary expansion and delabel patients with FPIES allergens may improve patient and family psychosocial functioning.[8]

There are potential downsides of home-based FPIES OFCs. There are no biomarkers for predicting FPIES resolution or identifying patients at risk of severe FPIES reactions that would require medical interventions, such as intravenous fluids or parenteral medications.[1] The optimal OFC location and protocol that balances time and safety is unknown.

The study by Sanders et al[5] is thoughtfully designed, provocative, and novel. They modeled 2 different scenarios to assess the cost-effectiveness of medically supervised OFC in individuals with mild-to-moderate index FPIES reactions and evaluated gradual home introduction vs medically supervised challenges in a population simulation and rural New England population. Fatality rates were estimated as 1/1,000,000 FPIES OFCs, and motor vehicle fatality rates were approximated by distance traveled to the facility. The cost-effective threshold was $10,000,000 per fatality avoided. In both simulations, the cost exceeded the value threshold for fatalities prevented in all permutations modeled. The authors concluded that for nonsevere FPIES index reactions, shared decision-making should be used when deciding where to conduct FPIES OFCs.

Study strengths include conforming to the Consolidated Health Economic Evaluation Reporting Standards, sensitivity analysis looking at emergency department visits and home-based OFCs, the addition of a rural New England cohort allowing for a real-world comparison using travel distance and costs, and permutations modeled.

Study limitations include lack of consideration of cost, stress, missed activities, and lost wages of families performing multistep food challenges at home and factors related to the heterogeneity of FPIES studies that can limit generalizability. The model assumes an 8% severe reaction rate based on 2 single-center studies of 39[9] and 169[10] FPIES OFCs, in which the median severity was mild in patients with classic FPIES. The model evaluated only infants with FPIES, so findings may not be generalizable to other age groups. The studies on which the model was based performed OFCs later than is typically recommended, perhaps resulting in lower severe reaction rates. The model did not consider atypical FPIES—which occurs in 25% of patients—in which IgE-mediated symptoms may occur and require alternate treatments with different outcomes.[1,2] Reasons for OFC, timing from last reaction, age, and population assessed could all affect reaction rates, so these a priori assumptions may not be generalizable to other FPIES populations.

Sanders et al[5] acknowledge the importance of shared decision-making when deciding where a challenge will take place, as not all families will find this practical and others may not be comfortable introducing an allergen at home. If home introduction is suggested, we do not know the best protocol to balance safety, time, and impact on the family.

Many home protocols, including the one proposed by Sanders et al,[5] start at low doses given over several days, with additional guidance on activity limitations and avoiding eating the allergen before

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bedtime. Multiday at-home protocols may be impractical for many families. For example, for many working parents, there is typically not a single weekday in which the family is home together for 4 hours before bedtime. Furthermore, monitoring for mild reactions with low doses could increase anxiety for some families. Counseling families on signs and symptoms of FPIES reactions, appropriate monitoring time, treatment, and necessary supplies such as oral rehydration and ondansetron to treat reactions is critical.[1] Using shared decision-making, alternative at-home OFC protocols using fewer or even single doses could be developed.

Having evidence-based support for at-home FPIES OFCs has potential benefits for many patients and families. Although not all families will be comfortable with this approach and all patients may not be appropriate, discussing the options with families seems reasonable. We owe our patients options and a discussion of risks and benefits, even if we do not have all the answers.

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