AAAAI Committee Paper

Allergist-Reported Trends in the Practice of Food Allergen Oral Immunotherapy

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What is already known about this topic? Results of promising preliminary studies indicate that oral immunotherapy (OIT) offers therapeutic potential. Although many thought leaders within the academic community strongly advocate for equipoise, a vocal minority of physicians in nonacademic practice advocate that it is ready for general use.

What does this article add to our knowledge? Minimal information exists regarding current practices for food OIT. This study reveals key differences in beliefs and concerns among those identifying as OIT providers and nonproviders and also differences in academic versus nonacademic OIT programs.

How does this study impact current management guidelines? Significant differences may exist with OIT that occurs in academic versus nonacademic settings. Opinions, motivations, and styles vary regarding regulatory oversight requirements, use of standardized product, and safety. Ongoing assessment is needed to understand these variations.

Food allergen oral immunotherapy (OIT) is an experimental, immune-modifying therapy that may induce clinical desensitization in some patients. OIT is still in early phase clinical research, but some providers may offer OIT as a clinical service. To understand the current practices of allergists who perform OIT, an online survey was sent by e-mail to members of the American Academy of Allergy Asthma & Immunology. Among 442 respondents, 61 reported participating in using OIT (13.8%), including 28 in nonacademic settings. Informed consent for OIT was obtained by 91.3%, institutional review board approval by 47.7% and Investigational New Drug approval by 38.1%. Compared with nonacademic participants, more academic participants used peanut OIT, obtained institutional review board and Investigational New Drug ($P < .0001$ respectively), and challenged patients before entry ($P = .008$). More nonacademic providers billed the patient or insurance for reimbursement ($P < .0001$). Low reported regard for the importance for US Food and Drug Administration approval or a standardized product (increased odds), and a high regard for better safety data (decreased odds) were associated with considering offering OIT as a service. Significant differences exist with OITs that occur in academic versus nonacademic settings. Further assessment is needed regarding the different motivations and practice styles among providers who offer OIT and those who are considering doing so. © 2014 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2015;3:33-8)

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Food oral immunotherapy (OIT) is an investigational treatment that can modulate the immune response[1,2] and has been shown in small trials to induce variable hyporesponsiveness to allergen (eg, clinical desensitization).[3-5] However, the interventions and end points used in these and other published trials vary widely, and, to date, most study designs either have not included controls or have used a cross-over design. As a result, neither safety nor efficacy have been definitively established as superior to allergen avoidance, and recent National Institutes of Allergy and Infections Diseases food allergy treatment guidelines specifically recommend against the use of OIT in clinical settings.[6] OIT also is not currently approved by

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Abbreviations used
AAAAI- American Academy of Allergy, Asthma & Immunology
CPT- Current Procedural Terminology
FDA- US Food and Drug Administration
IND- Investigational New Drug
IRB- Institutional review board
OIT- Oral immunotherapy
OR- Odds ratio

the US Food and Drug Administration (FDA), a convention that some allergists in private practice have contested as unnecessary given the potential benefits of OIT.[6-9] The question of equipoise in the practice of OIT continues to be prominently debated, in light of still emerging data that pertain to the safety and efficacy of OIT.[7,10-13] There are limited data that pertain to the actual practice of OIT outside of trials conducted at academic medical centers,[8,11,14] but it is known that OIT is being offered by allergists as well as otolaryngologists and nonallergy specialists in several states, with limited differentiation of these services by patients and some exploratory data suggestive that provider framing is a factor in influencing parent participation in OIT programs.[15]

Additional factors that have been shown to influence participation in using OIT at an academic center include parental anxiety and perception of reaction severity.[16] However, there are no current data that explored provider-level motivations to participate in using OIT, either in an academic or a nonacademic setting; provider opinions regarding OIT; and the question of equipoise as well as understanding the differences that may exist in current practice styles among providers who offer OIT. We, therefore, undertook a study to survey these provider-level attributes among members of the American Academy of Allergy, Asthma & Immunology (AAAAI), to better understand current practice styles and sentiment regarding OIT.

METHODS

A 23-question survey was developed by the investigational team through the AAAAI Adverse Reactions to Foods Committee Subgroup on Oral and Sublingual Immunotherapy. Membership on the subcommittee was open to any interested committee member. Questions were developed to survey current OIT practice styles (including types of patients, patient age, allergens for which OIT was offered, protocol and oversight, and reimbursement options for OIT), opinions on OIT practice styles and current regulatory climate, barriers to entry to the practice of OIT, awareness of other providers who are practicing OIT, and demographic information. Once developed, the survey was posted, for group feedback, on the Basecamp access site for the Adverse Reactions to Foods Committee. Once approved by the subcommittee, the survey was then forwarded to the AAAAI Needs Assessment Committee for approval before distribution through the AAAAI membership e-mail distribution list in January of 2013 to 4370 domestic and international members. A reminder e-mail within a 2-week period was sent to members who did not complete the survey within a specified time frame.

The survey was offered for 4 weeks. No financial incentive for participation was provided. The questions were administered in a multiple-choice format, with some questions that allowed for multiple responses per question, and selected questions that allowed for an open-ended additional response. Response to every question was not mandated. Responses were automatically tabulated through the Survey Monkey server (SurveyMonkey, Palo Alto, CA) and exported to a spreadsheet for data cleaning, variable labeling and/or coding, and uploading into a statistical package. Data were collected and analyzed at the provider level for general descriptive trends by using frequency analysis, and inferential proportional comparisons were assessed by using the 2-sided Fisher exact test at a prespecified alpha level of .05 for significance. Logistic regression was used to build an exploratory model of prespecified factors that may influence provider participation in using OIT. Data were analyzed by using Stata IC, Version 12 (Stata Corp, College Station, Texas). This study was deemed exempt from ongoing review by the University of North Carolina School of Medicine Institutional Review Board.

RESULTS

A total of 442 allergists responded to the survey (a response rate of approximately 10.1% of 4370 invitees). Among responding allergists (n = 440 to this question), 75.9% identified that they were in a private practice (96 in solo practice, 157 in a single specialty group practice, and 81 in a multispecialty group practice), and 24.1% were in an academic practice (106). Geographically, 18.3% reported practicing in the Northeast, 17.4% in the Mid Atlantic area, 10.5% in the Southeast, 17.6% in the Southwest, 17.6% in the Upper Midwest, 18.5% in the Far West, and 0.1% in Canada. Approximately 41.7% indicated that they were aware of either another allergist or another provider (including nonallopathic providers) offering OIT, and 42.6% were aware that another allergist or provider was offering sublingual immunotherapy to food (an alternative approach to oral tolerance also being researched or offered clinically).

A total of 61 providers (13.8%) indicated that they were providing OIT as a service or were studying OIT under a research protocol. Among the allergists who participate in using OIT in some capacity, 68.9% (42/61) reported obtaining informed consent before initiating OIT (including 88% of respondents in academic practice and 95% of those in private practice), 34.4% (21/61) reported having institutional review board approval to conduct OIT, 22.9% (14/61) reported that a data safety monitoring board oversaw their administration of OIT, 26.2% (16/61) reported obtaining an Investigational New Drug to administer OIT, and 18% (11/61) reported they had none of these aforementioned oversights in place. The location (venue) of where dose escalations occurred and the frequency at which dose escalations occurred are detailed in Figure 1. Forty-six respondents provided information regarding compensation for OIT, with 23.9% reporting research or grant funding, 43.5% reporting insurance reimbursement, 13% reporting that the patient paid out of pocket, and 19.6% reported offering the service *pro bono*. When asked to rank the relative importance of OIT as a means of developing a new revenue stream, however, 9.7% indicated that this was a "most important" or "very important" consideration, and that there was no significant difference in this trend when comparing academic and private practice. Specific differences with the administration of OIT between allergists who identified themselves as academic versus those who identified themselves as nonacademic are detailed in Table I.

Among the 381 providers not participating in using OIT currently, 74.3% indicated that they are awaiting FDA approval