

# Clinical Management of Plant Food Allergy in Patients Sensitized to Lipid Transfer Proteins Is Heterogeneous: Identifying the Gaps

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## ■ Abstract

**Background:** Patients sensitized to lipid transfer protein (LTP) are characterized by wide clinical variability. The lack of practical diagnostic and therapeutic guidelines complicates their management.

**Objective:** The aim of the study was to describe the clinical approach of Spanish allergists to sensitization to LTP.

**Methods:** We used a survey designed following the PICO method and subsequent validation using the Delphi approach.

**Results:** The survey was completed by 224 allergists (75% women; 57.1% with >20 years of professional experience). Clinical practice for the main points of diagnosis of LTP allergy was homogeneous, except for patients with suspected hypersensitivity to nonsteroidal anti-inflammatory drugs (44.6% frequently included skin testing with LTP). Oral food challenges were not frequently performed (63.6% occasionally to never) and were generally (75.5%) used to confirm tolerance.

It was common to recommend fruit skin avoidance (77.2%) and to maintain consumption of foods to which patients were sensitized but tolerant (99.1%). The results were heterogeneous for other dietary indications, modifications due to cofactors, and trace avoidance. Peach sublingual immunotherapy (SLIT) was considered very/quite effective by 55.9% of allergists. Most (79.5%) consider SLIT indicated in <25% of LTP-allergic patients based on severity (95.2%), frequency of reactions (99.4%), allergy to multiple food families (97.4%), and impairment of quality of life/nutrition (91.5%). Practice with respect to prescription of SLIT varied based on cofactor involvement.

**Conclusions:** These data suggest that there is a need to increase evidence to reduce heterogeneity in the clinical management of LTP allergy.

**Key words:** Avoidance diet. Diagnosis. Food allergy. Lipid transfer protein. Management. Peach allergy. Sublingual immunotherapy. Treatment.

## ■ Resumen

**Antecedentes:** Los pacientes sensibilizados a la proteína de transferencia de lípidos (LTP) presentan una amplia variabilidad clínica. La falta de guías clínicas prácticas diagnósticas y terapéuticas complica su manejo.

**Objetivo:** El objetivo de este estudio fue describir el abordaje clínico de esta patología por parte de los alergólogos españoles.

**Métodos:** Se aplicó una encuesta diseñada por el método PICO y posterior validación por método Delphi.

**Resultados:** La encuesta diseñada fue respondida por 224 alergólogos (75% mujeres; 57,1% con >20 años de experiencia profesional). Se observó homogeneidad en la práctica clínica en los principales puntos del diagnóstico de alergia a la LTP, excepto en los pacientes con sospecha de hipersensibilidad no inmunológica a AINE (el 44,6% evalúa frecuentemente la sensibilización a LTP en prueba cutánea). Las provocaciones orales a alimentos no se realizaron habitualmente (63,6% de vez en cuando a nunca) y, generalmente (75,5%), se utilizaron para confirmar la tolerancia a alimentos.

Fue práctica común recomendar la evitación de las pieles de frutas (77,2%) y mantener el consumo de alimentos a los que los pacientes están sensibilizados pero toleran (99,1%). Hubo heterogeneidad en otras indicaciones dietéticas, modificaciones debidas a cofactores o evitación de trazas. La inmunoterapia sublingual con melocotón (SLIT) fue considerada muy/bastante eficaz por el 55,9% de los alergólogos.

La mayoría (79,5%) considera que la SLIT está indicada en <25% de los pacientes alérgicos a la LTP, según la gravedad (95,2%), la frecuencia de las reacciones (99,4%), la alergia a múltiples familias de alimentos (97,4%), la afectación de la calidad de vida y deterioro nutricional (91,5%). La indicación en la prescripción de SLIT basada en la participación de cofactores fue heterogénea.

**Conclusiones:** Estos datos sugieren la necesidad de aumentar la evidencia en esta patología para reducir la heterogeneidad de la práctica clínica en el manejo de la alergia a la LTP.

**Palabras clave:** Dieta de evitación. Diagnóstico. Alergia alimentaria. Proteína de transferencia de lípidos. Manejo. Alergia a melocotón. Inmunoterapia sublingual. Tratamiento.

## Summary box

- **What do we know about this topic?**

Sensitization to lipid transfer protein (LTP) is expressed via different phenotypes. No practical guidelines are available, and current evidence is scarce. The clinical management of LTP-sensitized patients is heterogeneous.

- **How does this study impact our current understanding and/or clinical management of this topic?**

This study described the clinical approach of Spanish allergists to patients sensitized to LTP based on a survey and by analyzing agreement/disagreement. Areas for clinical improvement are identified, knowledge gaps are highlighted, and recommendations are given based on clinical practice and available evidence.

## Introduction

Lipid transfer proteins (LTPs) are widely distributed panallergens in the plant kingdom. They represent one of the leading causes of food allergy in adults in Southern Europe [1,2], particularly in Spain, although they have also been described as allergens in China [3] and in Northern Europe [4-6]. LTPs are found in a wide variety of foods, with higher concentrations in fruit and vegetable skins [7,8]. Peach LTP, Pru p 3, is the most allergenic LTP in the Mediterranean basin [1,9] and a common primary sensitizing agent [10,11].

Various patterns of sensitization to LTP have been reported depending on the following factors: (i) clinical presentation, from subclinical sensitization to reactions of variable severity; (ii) cross-reactivity between foods, with symptoms caused by only 1 food or even a single fraction of the food (eg, the skin, with tolerance of the pulp) or a multitude of foods, can trigger symptoms, resulting in so-called LTP syndrome [12]; (iii) cofactors, whose presence can, in some LTP-sensitized patients, trigger a reaction in a previously tolerated food (on/off effect) [13] or increase the severity of a pre-existing reaction (for example, a food causing oral allergy syndrome in a resting patient can cause anaphylaxis in the presence of a cofactor) [1,14]; and, finally (iv) disease progression in around one-third of LTP-sensitized patients, who develop symptoms with previously tolerated foods in long-term follow-up [15,16] (Figure 1). Recently, the European Academy of Allergy and Clinical Immunology (EAACI) Task Force published a review on the diagnosis and treatment of food allergy in patients sensitized to LTP [17]. The review highlighted the variability in sensitization profiles and clinical presentation and the lack of robust evidence in many aspects of sensitization to LTP.

Decision-making among allergists is heterogeneous owing to the complexity and clinical variability of LTP-sensitized patients, the lack of evidence supporting practical management guidelines, and differences in daily medical practice depending on available resources [18]. This study aims to describe the clinical management of LTP-sensitized patients in terms of both diagnosis and treatment in Spain, a country with high a prevalence of sensitization to this protein [19], and to analyze the degree of agreement in the practices carried out.

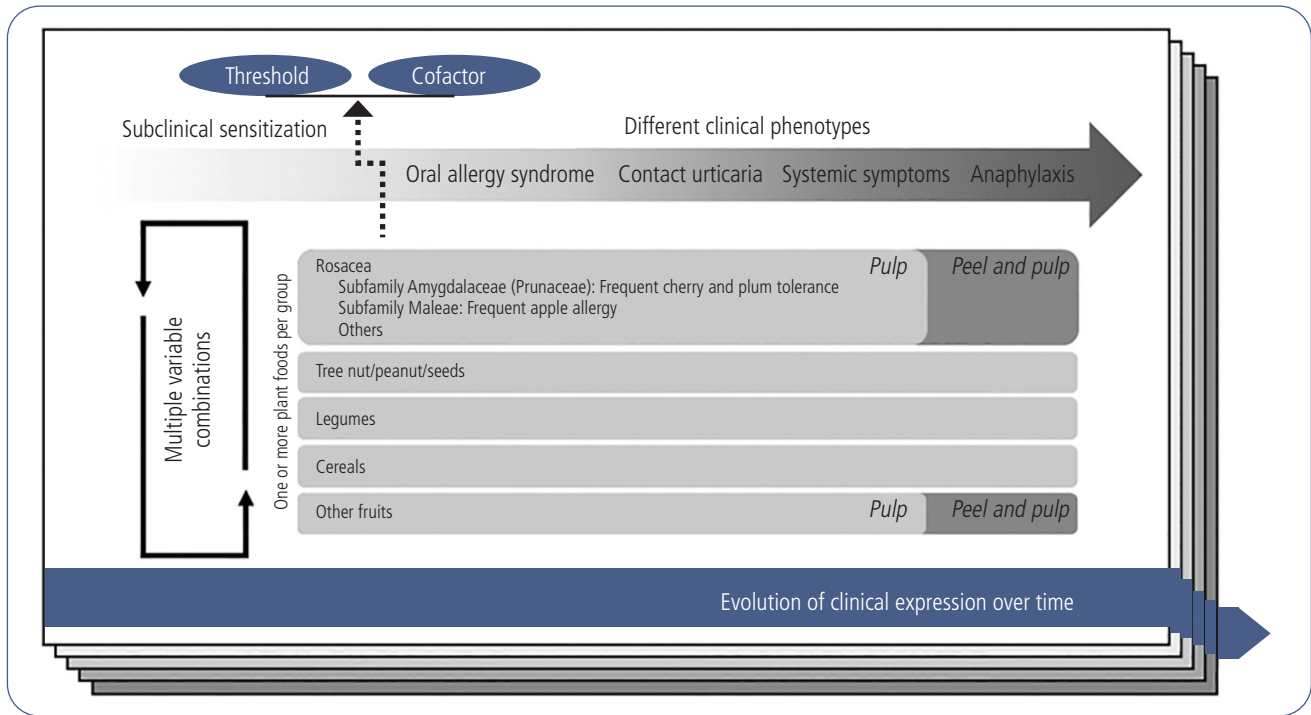
## Methods

### Study Design

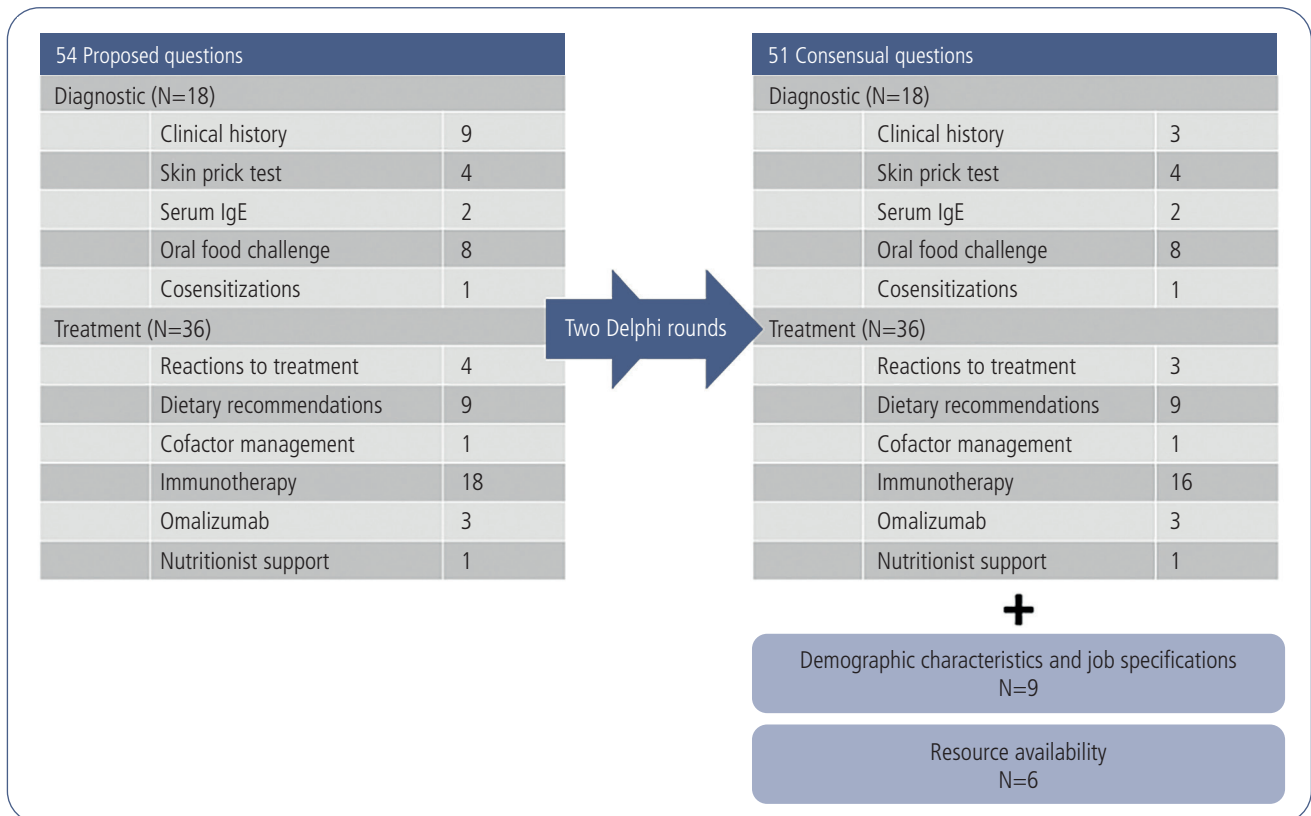
We performed an observational, exploratory, and descriptive study to collect data through an online survey on the usual clinical practice of allergists for LTP-sensitized patients. The survey was designed using the PICO format [20,21], and each question was validated using the Delphi approach (details of the survey design are available in the Supplementary Material). The survey resulted in 51 questions considered relevant by agreement (Table S2) (question selection flow diagram depicted in Figure 2). In a second phase, the survey was distributed to allergists in daily clinical practice and members of the Spanish Society of Allergy and Clinical Immunology (SEAIC). After analyzing the results and identifying possible inconsistencies, we rejected only 1 question (question 22 of Table S2).

### Statistical Analysis

Qualitative variables are presented as frequencies (percentages). The  $\chi^2$  test (or the Fisher exact test, when



**Figure 1.** Sensitization to LTP can manifest with lack of reactivity to plant foods or manifestations of different degrees of severity with different plant foods in the same individual. The fact that a high threshold or cofactors are required for the reaction in some cases could favor this duality of clinical response according to the amount of food and/or presence/absence of cofactors. The allergen LTP is present in many plant foods, and cross-reactivity is commonly observed. The absence of established clinical allergy cross-reactivity patterns with plant foods makes it difficult to predict reactions. Finally, it has been observed that food allergy and sensitization to LTP can evolve in some patients, leading to reactions with new plant foods.



**Figure 2.** Distribution by topic of proposed and selected survey questions.

**Table 1. Demographic Data of the Survey Participants.**

		<b>Allergists surveyed N=224</b>
Experience, y (4 y training included)	<5 y	6 (2.68%)
	5-9 y	28 (12.5%)
	10-20 y	62 (27.7%)
Female sex		168 (75%)
No. (%)		
Role in SEAIC		
LTP subgroup in Food Allergy Committee		14 (6.25%)
Food Allergy Committee, but not the LTP subgroup		14 (6.25%)
Not a member of the SEAIC Food Allergy Committee		196 (87.5%)
Workplace characteristics. Type of center		
Hospital-based		208 (92.9%)
Outpatient clinic		16 (7.14%)
Workplace characteristics. Management modality		
Public direct (managed by the health services of each Autonomous Community)		174 (77.7%)
Public - Other modalities (such as public companies, public foundations, and consortia)		12 (5.36%)
Private (through external contracting with the private sector)		38 (17.0%)
Origin of the population attended		
Rural		2 (0.89%)
Urban		63 (28.1%)
Rural and urban		159 (71.0%)
Age range of the population attended		
Pediatric population		9 (4.02%)
Adult population		67 (29.9%)
Pediatric and adult population		148 (66.1%)
Approximate number of patients sensitized to LTP seen per month		
<25		110 (49.3%)
25-50		96 (43.0%)
>50		17 (7.62%)
Available resources		
Purified LTP or LTP extract quantified for SPT		202 (90.17%)
Monocomponent specific IgE		211 (94.19%)
Allergenic protein platform for molecular diagnosis		140 (62.5%)
Oral food challenge		206 (91.96%)
Experience		
Oral food challenge performed in patients with suspected LTP allergy		205 (91.51%)
Pru p 3 sublingual immunotherapy use		165 (73.66%)

Abbreviations: LTP, lipid transfer protein; SEAIC, Spanish Society of Allergology and Clinical Immunology; SPT, skin prick test.

needed) was used to compare proportions. Answers were considered homogeneous when  $\geq 80\%$  agreement was achieved using the answer alone or taking together frequent and very frequent or never and rarely. Statistical analysis was performed using Stata/IC 12.0 software. A  $P$  value  $< .05$  was considered significant.

## Results

### Characteristics of the Allergists Surveyed

The survey was completed by 224 active allergists of the 1056 specialist members of the SEAIC at the time of the survey (November 2021-January 2022). Seventy-five percent of respondents were women, and more than half had several

**Table 2. Widespread Clinical Practice in Patients Sensitized to LTP.**

<b>Clinical Practice</b>	<b>Degree of homogeneity</b>
Patients with LTP allergy are systematically questioned about the involvement of cofactors in the reaction.	98.70%
Patients with sensitization/allergy to LTP are directly asked about their tolerance to foods frequently involved in LTP syndrome.	99.60%
In patients with sensitization/allergy to LTP, the use of a questionnaire to assess tolerance to different foods is considered useful but not commonly used.	86.20%
Skin prick test with purified LTP or LTP-quantified extract is routinely performed in the screening of patients with suspected food allergy.	94.60%
Specific IgE to individual LTP allergens is frequently or commonly determined in the diagnosis of patients with suspected sensitization/allergy to LTP.	94.79%
An adrenaline autoinjector is prescribed to patients with LTP allergy and anaphylaxis	100%
Patients allergic to a plant food owing to LTP are not advised to avoid foods to which they are sensitized and currently tolerate.	99.11%
Patients allergic to any food owing to LTP allergy are not instructed to avoid a fixed list of foods.	97.32%
Specific immunotherapy prescription in patients with LTP allergy is based on criteria of severity and frequency of reactions, allergy to multiple families, and impairment of nutrition and/or quality of life.	91.52%-99.39%
The intention of prescribers of specific immunotherapy to patients with LTP allergy is to expand the diet and reduce the number of reactions.	88.49% and 99.39%, respectively
Omalizumab is used exceptionally in patients with LTP allergy.	81.72%

Abbreviation: LTP, lipid transfer protein.

years of experience (57.1% over 20 years of experience) and were working in a public hospital (92.9%). Most respondents attended both pediatric and adult patients (66.1%), and more than 25 patients were sensitized to LTP per month (51%). Most allergists surveyed were not part of the SEAIC Food Allergy Committee (87.5%) (Table 1).

### General Survey Results

The survey revealed considerable disparity in the management of patients sensitized to LTP, since only one-third of the questions answered (33.3%) were considered homogeneous (Table 2).

### Diagnostic Work-up

Nearly all specialists took a detailed clinical history, with systematic questioning about involvement of cofactors in reactions (98.7%) and specific questioning about tolerance to other foods related to LTP syndrome that are not spontaneously reported (99.6%), following the recommendations of guidelines and experts [17,22]. However, they did not collect data on tolerance and habitual intake of a list of foods (91.5%), although they considered it would be useful (94.6%).

As for food allergy screening, purified LTP or LTP-quantified extract was systematically used for skin prick testing (SPT) by 96% of the specialists surveyed. Additionally, 48.7% of the respondents reported routinely conducting SPTs with predetermined food panels.

There was considerable variability in the use of enriched peach extract or purified LTP for SPTs in patients with suspected respiratory allergy (57.4%) and in patients with suspected hypersensitivity to nonsteroidal anti-inflammatory drugs (NSAIDs) (44.6%). Skin testing with LTP in patients with suspected hypersensitivity to NSAIDs was more frequent among allergists belonging to the LTP subgroup of the SEAIC Food Allergy Committee ( $P=.007$ ) and by those who attended a higher proportion of patients sensitized to LTP ( $P=.024$ ) than by the remaining respondents. More than a half of the respondents (57.6%) did not modify the management of their patients depending on cosensitization to profilin and/or PR-10, although data from the literature suggest a possible decrease in the risk of reactions in patients sensitized to LTP and profilin or PR-10 [23,25].

Only 36.4% of respondents frequently performed oral food challenges (OFCs) in patients with suspected LTP allergy. OFCs were predominantly performed (75.5%) to assess food tolerance as an exclusion diagnosis. Only 42% of respondents sought to expand the diet by challenging with foods to which patients were sensitized with unknown tolerance, and 50% frequently performed OFCs with foods implicated in the reaction with negative diagnostic tests. More than half of the respondents (56.7%) did not recommend free consumption at home of foods with negative SPT results not consumed recently. The frequency of OFCs was limited by the lack of confidence in real-life reproducibility in only 33.9% of respondents, while 66.1% considered that OFCs were limited by the lack of resources, especially among respondents who worked in public centers ( $P=.004$ ). Controlled exposure tests with cofactors were infrequent (16.5%).

### Management of Reactions

Absolute homogeneity was recorded for including an adrenaline autoinjector in the emergency kit of patients with LTP allergy and severe symptoms (100%). Prescribing adrenaline was almost homogeneous in LTP-allergic patients with moderate symptoms (77.2%). Interestingly, 9.82% of respondents prescribed an adrenaline autoinjector for patients with subclinical sensitization, and this indication was more frequent among respondents working in private health care settings than in public ones ( $P=.002$ ).

### Dietary Recommendations

Findings were heterogeneous for additional dietary recommendations beyond the avoidance of plant-foods implicated in reactions with demonstrated sensitization. Thus, 64.7% of the allergists surveyed also recommended avoiding foods for which sensitization with unknown tolerance was observed. However, a fixed list of foods was not usually indicated to be avoided (97.3%). The same was true for plant foods for which sensitization with known tolerance was observed (99.1%). Regular consumption of tolerated foods the patient was sensitized to was frequently or very frequently recommended by 76.8% of the respondents, albeit avoiding cofactors. Most of the respondents recommended avoiding fruit peel (77.2%), consistent with the higher concentration of LTP in this part of the fruit [8,26]. Recommendations regarding the avoidance of trace allergens were highly heterogeneous, with 31.7% frequently or very frequently recommending avoidance and the 42.9% never or rarely recommending avoidance.

It seems that the allergists surveyed were aware of the importance of cofactors in food allergy resulting from sensitization to LTP, since most of them informed the patient about cofactors, either only verbally (23.7%) or verbally and in writing (74.1%). Half of the allergists (50.9%) made different recommendations for avoiding certain foods or parts of them depending on cofactor involvement in the index reaction.

### Immunomodulatory Treatment

Sublingual immunotherapy based on peach peel extract enriched with Pru p 3 (ALK-Abelló) (SLIT-peach) was perceived as very or quite effective by only 55.8% of respondents, although 73.7% of specialists reported experience using it. For three quarters of the respondents (75%) this treatment would be indicated in 1% to 25% of LTP-mediated plant food-allergic patients. According to more than 90% of the prescribers, the prescribing criteria were severity of symptoms, frequency of reactions, allergy to multiple food plant families, and quality of life/nutritional impairment. Cofactor involvement was important or very important in SLIT-peach prescription for 60% of allergists prescribing it.

The main barrier to prescription of SLIT-peach was patient refusal for most of those interviewed (74.5%). In fact, treatment was frequently or very frequently rejected by patients according to 26.6% of the 165 prescribers. Other reasons for rejection were its cost (58%) and duration (42%). The lack of knowledge of SLIT-peach was a significant barrier to its prescription in 39.7% of the allergists surveyed.



Moreover, the data showed prescription of omalizumab to be residual in patients with LTP allergy (Table S2).

## Discussion

This study was designed to assess the degree of agreement in the management of patients with LTP allergy or sensitization, given the complexity of the condition, the lack of available evidence, and the absence of specific clinical guidelines on practical management. The EAACI Task Force on patients sensitized to LTP [17] focused mainly on the diagnosis of LTP allergy, highlighting the need for increased evidence in problems associated with the clinical management of affected patients. Our survey, on the other hand, focuses specifically on clinical management (33/51; 64.7% of questions in the survey) rather than on diagnosis (16/51; 31.4%).

Diagnosis of LTP allergy involves identifying an IgE-mediated reaction and sensitization to LTP (SPT and/or serum IgE). It has been observed that allergy to a specific vegetable due to its LTP is limited to certain foods, and a negative test result for Pru p 3, the most frequent LTP and often the primary sensitizing agent [1,10-11,27], may not exclude a diagnosis of LTP allergy owing to the absence of universal cross-reactivity between them [28]. However, the high sensitivity and specificity of IgE to Pru p 3 and SPTs with enriched or purified LTP extracts [6,29,30] support their application in suspected LTP allergy, with the result that they were widely used by the allergists surveyed. Nevertheless, although sensitization to multiple food groups without an established clinical cross-reactivity pattern and the possible appearance of reactivity to new foods would lead to a high number of OFCs to achieve an accurate diagnosis, the use of OFCs, according to two-thirds of the allergists surveyed, appears to be limited owing to a lack of resources. Additionally, even though the lack of evidence on reaction thresholds and cofactor involvement could be limiting for OFCs, the lack of real-life reproducibility seems to be a limiting factor for only a third of the respondents.

These data suggest that there is little confidence in the absence of reactivity to plant-based foods with negative SPT results in patients with suspected LTP allergy, since, despite occasional use of OFC, half of the respondents reported using this approach frequently with foods involved in the reaction without sensitization. In addition, introducing these foods at home with negative diagnostic test results and no recent evidence of tolerance was only indicated by less than half of the respondents. In this sense, the EAACI Task Force reported the usefulness of OFC in sensitized LTP patients with positive results for specific foods [17]. In fact, the indication of OFC for foods with negative SPT results does not seem to be necessary, since the main problem with diagnostic tests in LTP allergy is the low positive predictive value [6,30]. It is interesting to note that 1 in 10 respondents prescribe adrenaline to LTP-sensitized patients without previous reactions. The combination of OFC using foods with negative diagnostic test results and the prescription of adrenaline in sensitization with no previous clinical reactions suggests that the allergists surveyed are concerned about this disease.

Introduction of new foods to achieve less restrictive diets seems to be difficult, since more than half of the allergists

surveyed did not routinely perform OFCs with foods leading to sensitization with unknown tolerance. However, almost all respondents agreed not to forbid foods the patient was sensitized to but tolerated in daily life, and most encouraged frequent consumption of these foods with avoidance of cofactors. In fact, the importance of cofactors is underscored by the fact that the respondents provided information on cofactors verbally and in writing in most cases. In contrast, more than half of the respondents did not consider the inclusion of LTP in the screening for suspected hypersensitivity to NSAIDs in a country with a high prevalence of sensitization to LTP (Spain) [19], as previously proposed [15].

The EAACI Task Force stated that dietary restriction should be individualized based on reactions experienced, foods habitually consumed, and taste preferences [17]. Cofactors should also be considered. Nevertheless, robust evidence on whether cofactor susceptibility is predetermined and can be ruled out in specific patients is lacking [31]. The EAACI Task Force also discussed the possibility of avoiding the most likely reactive foods and encouraged the ingestion of relatively safe ones [17]. Wide restriction of other foods is frequent in Spain, since it is advised to avoid foods causing sensitization with unknown tolerance, foods from the same taxonomic family assuming high cross-reactivity between them [32] (although tolerance can be variable between foods of the same group [33]), and the skin of fruits in general [26]. This approach presumably increases safety in a scenario of sensitizations of uncertain clinical relevance, limited indication of OFCs, and the possible risk of future reactions to new foods, as reported in 1 out of 3 patients [15,16]. However, since many data are missing, 2 questions necessarily arise from these studies. First, the origin of these new food allergies due to LTP allergy is unknown and could result from the transformation of subclinical sensitization into clinical sensitization or from new clinically relevant sensitization. And second, it is not known whether the emergence of new symptomatic foods depends on consumption habits (frequent vs sporadic). These additional restrictions, if systematically recommended, would hypothetically reduce the risk of new reactions at the expense of impaired quality of life in LTP-allergic patients, possibly owing to unnecessary restrictions. Furthermore, our data suggest that maintaining frequent consumption of foods for which sensitization is subclinical is the best way to preserve tolerance, at least while avoiding cofactors, although there are no robust scientific data to support this hypothesis [16,34,35].

Since 2015, SLIT-peach (ALK-Abelló) has been marketed only in Spain, with a reported increase in the reaction threshold for peach with peel and other symptomatic foods, a reduction in the severity of reactions and immunological changes, and good tolerance [36-40]. However, although the evidence is insufficient, mainly owing to the low number of patients included in the pivotal trial [41], both the latest European guideline on immunotherapy [42] and the EAACI Task Force on LTP allergy [17] mentioned the efficacy reported in the literature, endorsing this approach in some patients. In our sample, almost 3 out of 4 allergists surveyed have some experience in the use of SLIT-peach in LTP-allergic patients, although this therapy is not perceived to be very effective (55% of respondents consider it very or quite effective). In any case, a very high percentage of respondents restrict SLIT-peach to

**Table 3.** Areas of Interest for Future Research in Management of the LTP-Sensitized Patient**Practices to be improved**

In areas with a high prevalence of sensitization to LTP and susceptibility to cofactors, it seems advisable to screen for LTP allergy in reactions to nonsteroidal anti-inflammatory drugs.

In LTP-sensitized patients, there is no evidence for distrusting tolerance to foods with negative results in skin prick test (prick or prick-prick) and specific IgE.

In LTP-sensitized patients, oral food challenge should preferably be performed when there is no clear involvement in a previous reaction for foods the patient is sensitized to compared with those for which test results are negative.

**Evidence needs**

Identification of risks factors for developing new food allergies in patients sensitized to LTP.

Identification of biomarkers predicting susceptibility to cofactors.

Convenience of indicating frequent consumption of foods the patient is sensitized to

Development and validation of questionnaires on tolerance/reactivity or precautionary avoidance of foods in patients sensitized to LTP.

Increasing evidence of the efficacy of peach sublingual immunotherapy in patients with allergy to LTP

Evaluation of the efficacy of peach sublingual immunotherapy in cofactor-dependent reactions

Role of peach sublingual immunotherapy in the appearance of new clinical reactivity with new foods

Abbreviation: LTP, lipid transfer protein.

a minority of LTP-allergic patients (<25%), namely, those with more severe disease and more frequent reactions and/or a greater number of symptomatic foods, aspects in which efficacy has been demonstrated. In fact, a 6-month course of SLIT-peach reduced the frequency of systemic reactions by 50% and increased the reaction threshold by 3 to 9 times [36]. Moreover, in 1 year, tolerance increased to a significant amount of unpeeled peach in 95% of treated patients, compared to the untreated group [37,40]. Homogeneous prescription seeks to improve these aspects of severity and frequency of reactions, as well as patients' quality of life, as reported elsewhere [43], and to prevent new allergies, as suggested by Beitia et al [40]. Despite homogeneity with respect to the importance of cofactors in diagnosis, only 60% of respondents consider their frequency important or very important when prescribing SLIT-peach, probably because the role of this treatment in controlling them has not been studied.

One potential limitation of our study is the low participation in the survey (21.2% of those invited), which could affect the representativeness of the sample owing to a possible selection bias: respondents who may show greater interest in sensitization to LTP than nonparticipating allergists. Another limitation of the study is the use of closed questions, which do not allow for a detailed analysis of the factors that determine decision-making. Furthermore, it is important to consider that

the heterogeneous management of patients sensitized to LTP could be due to the variability in the condition itself more than heterogeneity in clinical practice. This is an exploratory study that aimed to address the current situation, from diagnosis to proactive dietary treatment, as a starting point from which targets of interest for future research can be identified (Table 3).

In conclusion, heterogeneity in the management of patients sensitized to LTP was observed in two-thirds of the questions presented to allergists in a country where sensitization to this protein was highly prevalent. Our findings revealed several areas for improvement, such as the inclusion of SPT with LTP in adverse reactions to NSAIDs and optimizing the use of limited resources, such as OFCs, by conducting them with foods to which the patient is sensitized, as opposed to those for which diagnostic test results are negative. Practices are conflicting, especially regarding dietary recommendations, likely owing to the lack of robust evidence and concern about the disease perceived in the survey. In LTP-sensitized patients with food allergy, the available evidence indicates that we can recommend avoidance of foods involved in reactions associated with sensitization, foods the patient is sensitized to with unknown tolerance, and foods with proven tolerance but for which consumption is not guaranteed and cofactors may not be avoided. More evidence on the process of sensitization to LTP, clinical presentation, and outcomes after SLIT-peach could help to reduce heterogeneity in the management of LTP allergy.

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**Conflicts of Interest**

The authors declare that they have no conflicts of interest.

### Previous Presentation

Preliminary results of this work were presented as an oral communication at the 2022 SEAIC meeting “International Symposia on Personalized Allergology: Immunotherapy and Allergy to Drugs” held in Palma de Mallorca, Spain, October 2022.

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