ORIGINAL ARTICLE

Sunflower (*Helianthus annuus*) Seed Allergy

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Abstract

Background: Sunflower seed is one of the most common edible seeds. Its consumption is growing. Cases of sunflower seed allergy have been reported since the 1970s. However, there are few data on the prevalence and clinical manifestations of sunflower seed allergy.
Objective: To improve our understanding of sunflower seed allergy.
Methods: We evaluated the clinical and immunological features of patients with sunflower seed allergy diagnosed in the allergy department of a tertiary hospital in Madrid over a 5-year period.
Results: Forty-seven patients reported adverse reactions after ingestion of sunflower seed and were sensitized specifically to sunflower seed, as determined by skin prick test (median, 8 mm) or specific IgE (median, 1.10 kU_A/L). Most reactions were adult-onset and were preceded by a history of atopy and other food allergies, predominantly to peach, peanut, and nuts. The clinical presentation of sunflower seed allergy ranged from mild to severe, with many patients experiencing severe reactions, in which epinephrine was underused. Repeated exposures to sunflower seed in the same patient showed severity of symptoms to vary. Levels of sunflower seed IgE were strongly correlated with levels of IgE to nonspecific lipid transfer proteins, while the severity of the reactions did not differ significantly according to sensitization to the proteins.
Conclusion: Our findings reveal variability in the clinical presentations of sunflower seed allergy on repeated exposures and underuse of epinephrine in anaphylaxis. We highlight the importance of strict avoidance of sunflower seed and accurate prescription and administration of epinephrine in allergic patients.

Key words: Sunflower seed. Food hypersensitivity. Severity. Skin prick test. Specific IgE.

Resumen

Antecedentes: La semilla de girasol es una de las semillas comestibles más frecuentes y su consumo está creciendo. Desde los años 70 se han descrito casos de alergia a las semillas de girasol. Sin embargo, hay pocos datos sobre la prevalencia y las manifestaciones clínicas de la alergia a la semilla de girasol.
Objetivo: Mejorar la comprensión de la alergia a la semilla de girasol.
Métodos: Evaluamos las características clínicas e inmunológicas de pacientes con alergia a la semilla de girasol diagnosticados en el Servicio de Alergología de un hospital terciario de Madrid durante un periodo de 5 años.
Resultados: Cuarenta y siete pacientes reportaron reacciones adversas tras la ingesta de semillas de girasol y presentaron sensibilización a semilla de girasol determinada mediante prueba cutánea (mediana 8 mm) o IgE específica (mediana 1,10 kU_A/L). La mayoría de las reacciones se iniciaron en la edad adulta, precedidas de antecedentes de atopia y otras alergias alimentarias, predominantemente a melocotón, cacahuete y frutos secos. Las manifestaciones clínicas de la alergia a la semilla de girasol variaron de leves a graves, con una alta proporción de pacientes con reacciones alérgicas graves, y una infrautilización de adrenalina. En un mismo paciente, la gravedad de los síntomas varió en exposiciones repetidas a semillas de girasol. Se objetivó una fuerte correlación entre los niveles de IgE de semilla de girasol y los niveles de IgE a proteínas de transferencia de lípidos no específicas, sin encontrar asociación entre el grado de sensibilización a estas proteínas y la gravedad de las reacciones.
Conclusión: Los resultados revelan una variabilidad en las manifestaciones clínicas de la alergia a la semilla de girasol en exposiciones repetidas y una infrautilización de adrenalina en la anafilaxia. Destacamos la importancia de la evitación estricta del consumo de semillas de girasol y la adecuada prescripción y administración de adrenalina en los pacientes alérgicos.

Palabras clave: Semilla de girasol. Hipersensibilidad a alimentos. Gravedad. *Prick test*. IgE específica.

Summary box

- **What do we know about this topic?**
  Increasing consumption of seeds is leading to more frequent seed allergy. However, there are few data on the prevalence and clinical manifestations of sunflower seed allergy.
- **How does this study impact our current understanding and/or clinical management of this topic?**
  Our findings reveal variability in the clinical presentations of sunflower seed allergy on repeated exposures and underuse of epinephrine in anaphylaxis. We highlight the importance of strict avoidance of sunflower seed and accurate prescription of epinephrine in allergic patients.

Introduction

Sunflower (*Helianthus annuus*) is a genus of plants in the Asteraceae family. The edible seeds of the sunflower plant are commonly consumed in snacks, breads, and oils [1] and are the most popular snack eaten while attending football matches in Spain and many other European countries.

With the inclusion of seeds in many foods, the consumption of edible seeds, such as sunflower, sesame, mustard, poppy, pumpkin, and flax, is growing worldwide; consequently, the prevalence of allergy to seeds is increasing [1-7]. Sesame seems to be the most common cause of seed allergy, with a worldwide prevalence of sesame allergy between 0.1% and 0.2% [3]. The prevalence of sensitization to sunflower seed in Europe was investigated in the EuroPrevall project by averaging the prevalence over different centers from each country. The authors reported a prevalence ranging from 0% in countries such as Iceland to 1.9% in Spain and 4.8% in France [7], possibly owing to differences in dietary habits. However, the overall prevalence and clinical manifestations of sunflower seed allergy have yet to be fully examined.

Despite frequent consumption, and since the first sunflower seed allergy reported by Noyes et al [8] in 1979, publications on sunflower seed allergy have been limited to case reports or case series with a small number of patients [1-21].

This study sought to evaluate the clinical and immunological features of IgE-mediated hypersensitivity to sunflower seed and other food allergies in sunflower seed–allergic patients.

Methods

Patients

A retrospective case series study was conducted in the Allergy Department of Hospital Universitario 12 de Octubre, Madrid, Spain over 5 years. The inclusion criterion was clinical reactivity to sunflower seed, that is, adverse reactions on exposure to sunflower seed confirmed by demonstrating specific sensitization. Forty-seven patients with clinical reactivity to sunflower seed were evaluated. Informed consent was not required owing to the retrospective nature of the study and the anonymization of clinical data. The study was approved by the Ethics Committee of Hospital Universitario 12 de Octubre (Approval No. 19/554).

Diagnostic Procedures

First, we collected a series of data, namely, history of atopy, food reactions, other comorbidities, number of reactions to sunflower seed, age at first reaction, symptoms, route of exposure, time between exposure and onset of symptoms, treatment in the emergency department, and medications used to treat the reactions.

Second, we recorded the results of the skin and in vitro diagnostic tests performed in our center.

Skin prick tests (SPTs) and prick-prick tests (P-Ps) were performed according to the standard technique by trained health care professionals. P-Ps were performed using fresh sunflower seeds, peanuts, nuts (walnut, almond, hazelnut, pistachio, cashew, pine nut, and chestnut) and other culprit foods recorded in the patients' clinical history. SPTs were performed with commercially available panallergen extracts, including profilin (LETI) and peach extract (ALK-Abelló), which contains 30 mg/mL of the nonspecific lipid transfer protein (nsLTP) Pru p 3. Positive results in P-P and SPT were defined as a wheal size at least 3 mm greater than the negative control. Histamine and saline (ALK-Abelló) were used, respectively, as positive and negative controls.

Total IgE and specific IgE against sunflower seed, peanuts, nuts, other foods, and panallergens were measured

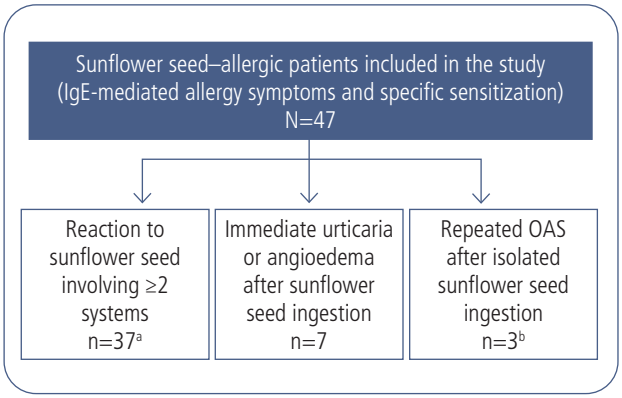

Figure 1. Clinical classification of 47 sunflower seed–allergic patients. OAS indicates oral allergy syndrome.
[a]In 2 patients, the diagnosis was confirmed by positive double-blind placebo-controlled oral food challenge and a positive open food challenge with sunflower seed.
[b]In 1 patient, the diagnosis was confirmed by a positive double-blind placebo-controlled oral food challenge.

Table 1. Demographic Features, Symptoms After Sunflower Seed Ingestion, Skin Test and Specific IgE Results, and Other Previous Food Allergies in 47 Patients With Sunflower Seed Allergy.

No.	Sex	Age	Symptoms (WAO)[a]	P-P to SS, mm		Specific IgE to SS and food proteins, kU_A/L								Food reactions previous to SS	
						SS	Ara h 2	Ara h 9	Jug r 1	Jug r 3	Cor a 8	Pru p 3	Pru p 4	Peanut/Nuts	Other foods
1	F	41	1			1.9						42.6			Pc, Pl, Av, K, Ba
2	M	40	3	+	20	3.0		2.1							Cru
3	F	42	3	+	5	40.3	0.1	88.4	0.0	53.6	16.4	57.3			K
4	M	26	3	+	11	2.9	0.0	7.0	0.0	3.9	2.7	8.8		Al	K
5	F	57	3	+	4	12.7	0.0	54.3		19.9	5.4	59.4	0.1	Pn	Pc
6	F	27	3	+		8.8	0.0	15.0	0.0	9.3	5.2	13.4	0.0		Pc
7	M	21	3	+	22	0.4	0.0	0.4	0.0	0.6	0.3	0.7			Pc
8	M	45	3	+	11	0.6									
9	F	26	3	+	11	3.0		3.2			1.3	5.3	1.2	Pn, Hn, Cn, Al	
10	M	25	3	+	5	0.7	0.0	1.8	0.0	1.2		2.2	0.0		
11	F	63	4	+	11	2.8	0.0	7.8	0.0	6.9	4.5	11.8			
12	M	42	2	+	8	1.2	0.0	1.2	0.0	1.4				Pn, Hn	
13	M	26	3	+	11	1.7	0.0	4.6	0.0	3.6	3.3				
14	F	48	3	+	9	0.7	0.0	0.0			0.0				
15	M	28	3	+	4	9.4	0.1	28.7				26.9	2.3		
16	M	68	3	+	9	0.2	0.0	0.0	0.0	0.0	0.0				
17	F	37	2	+	5	0.8	0.0	1.8	0.0	1.6	1.2	2.1	0.0	Ps	Pc
18	M	40	1	+	7	2.3			0.0	1.4	0.0				
19	M	42	2			1.2									
20	M	41	5			1.0								Pn, Wn, Hn	
21	M	24	3	+	12	2.3						11.4	0.0	Wn, Pi	Pc, Apr, St, K, To
22	M	33	1	–		0.5						10.3	0.5	Pn	Pc
23	M	31	1	+	9	3.1	0.0	4.4	0.0	4.9	2.1	9.2		Pn	Pc
24	F	21	2	+	5	2.9		7.2	0.0	8.9	6.0	12.0		Pn, Wn	Pc
25	F	23	3			4.1	0.0	9.5	0.0	8.4	3.7	10.9	0.1	Pn, Hn, Wn	
26	M	20	2			2.1						5.2	0.0	Cn	Pc, To
27	M	41	2	+	8	0.4					0.0			Ps	Ma, Cu
28	F	27	1	–		2.0	0.0	3.8	0.0	3.6	1.5				Pc, Mu-S
29	F	37	3	+	15	24.3	0.0	0.0	0.0	0.0	0.0	0.0		Hn	
30	M	16	2	+	7	2.2	0.1	0.1	0.2	0.1	0.1				
31	F	49	2	+	5	1.0	0.0	2.3	0.8	0.7	0.2				
32	F	44	2	–		0.9	0.0	0.0	0.0	0.1	0.1	0.1		Pn, Ps, Hn, Al	
33	F	36	1			0.4	0.0	1.7	0.0	1.2	0.4			Wn, Al	
34	F	17	2	+	9	0.2								Pn, Wn, Hn, Al	To, Gb, Wb
35	M	42	1	–		8.2								Hn	App
36	F	30	2	+	6	1.1	0.0	0.0	0.0	0.0	0.0	0.0		Pn, Wn, Al, Hn, Ps, Pi, Cn	Pc, App, Pl, Ch, St, Av, On, Ga, Ba, Me, Wm, O, Le, To, Lt, Sp

(continued)

Table 1. Demographic Features, Symptoms After Sunflower Seed Ingestion, Skin Test and Specific IgE Results, and Other Previous Food Allergies in 47 Patients With Sunflower Seed Allergy (*continuation*).

N	Sex	Age	Symptoms (WAO)[a]	P-P to SS, mm		Specific IgE to SS and food proteins, kU_A/L								Food reactions previous to SS	
						SS	Ara h 2	Ara h 9	Jug r 1	Jug r 3	Cor a 8	Pru p 3	Pru p 4	Peanut/Nuts	Other foods
37	M	24	1	+	10	1.5									
38	F	46	2	+	20	0.8								Pn, Al, Wn	Pc
39	F	51	3	+	6	0.5	0.0	4.4	1.4	2.0	0.8	3.4	0.8		
40	F	25	1	+	5	0.0			0.0	0.0		0.0			
41	F	65	3	+	8	0.0			0.0	1.1	0.4	1.3			Pc
42	F	45	3	+		0.1									
43	F	18	1	+	6	0.1	0.0	0.3	0.0	3.4	0.0	8.0	0.0	Pn, Wn, Al	Pc, App, Ch, Pr, Le
44	F	41	3	+	3	0.1		0.4	0.0	0.2		0.8		Wn	Pc, Me
45	F	27	2	+	5	0.1	0.0	0.0						Pn, Wn, Pi, Ps	Pl, Ch
46	M	32	5	+		0.1									
47	M	16	2	+	6	0.2	0.0	0.5	0.0	1.3		3.3	0.0	Wn	

Abbreviations: Al, almond; App, apple; Apr, apricot; Av, avocado; Ba, banana; Ch, cherry; Cn, chestnut; Co, coconut; Cru, crustaceans; Cu, curry; Ga, garlic; Gb, green bean; Hn, hazelnut; IgE, immunoglobulin E; K, kiwi; Le, lemon; Lt, lettuce; Ma, mango; Me, melon; Mu-S, mustard seed; O, orange; On, onion; P-P, prick-prick test; Pn, peanut; Pr, pear; Wn, walnut; Ps, pistachio; Pi, pine nut; Pc, peach; Pl, plum; Sp, spinach; SS, sunflower seed; St, strawberry; To, tomato; Wb, white bean; Wm, watermelon.
[a]Symptoms were graded according to the WAO systemic allergic reaction grading system. In patients with multiple reactions to sunflower seed, the most severe reaction was considered.

using ImmunoCAP (Thermo Fisher Scientific) following the manufacturer's instructions. Within the nsLTP group, specific IgE to rPru p 3, rAra h 9, rJug r 3, and rCor a 8 was determined. Specific IgE to other recombinant proteins, such as profilins (rPru p 4) and 2S albumins (rAra h 2 and rJug r1), was also evaluated. Specific IgE levels above 0.35 kU_A/L were considered positive.

Allergy was defined according to the European Academy of Allergy and Clinical Immunology (EAACI) Food Allergy and Anaphylaxis Guidelines [22]. The diagnosis of sunflower seed allergy was confirmed by IgE-mediated symptoms on exposure to sunflower seed and specific sensitization (Figure 1). Reactions were classified according to the World Allergy Organization (WAO) Systemic Allergic Reaction Grading System [23] into 5 grades based on the organs or systems involved and the severity of the reaction.

Specific sensitization to sunflower seed was demonstrated in all patients through skin tests and/or specific IgE. Clinical reactivity was confirmed by food challenge in 3 patients, including 2 double-blind placebo-controlled oral food challenges and 1 open food challenge.

Statistical Analysis

Descriptive statistics of the quantitative variables were reported as the number of patients and median (IQR). Qualitative variables were reported as frequency distributions (absolute and relative). Inferences were estimated depending on the nature of the variables using the χ^2 test or Fisher exact test for categorical variables and the Mann-Whitney or Kruskal-Wallis test for continuous variables. The correlation between severity of reactions to sunflower seed and IgE levels to sunflower seed and other allergens was measured using the Spearman rank correlation. All analyses were performed using Stata Intercooled for Windows (StataCorp. 2019. Stata Statistical Software: Release 16), with a significance level of 5%. A P value <.05 was considered statistically significant.

Results

We evaluated 47 patients with sunflower seed allergy (median age, 36 years; male/female ratio, 0.88). Table 1 shows their demographic features, symptoms, skin tests, specific IgE to sunflower seed and food proteins, and previous food allergies.

Clinical Features

Onset of symptoms was mostly in adulthood. Twelve patients (25%) reported onset at age <18 years. Onset was before 18 years in 43% of patients who reported sunflower seed allergy as their first food reaction, compared to 16% of patients with previous food allergies (P=.013).

Clinical manifestations appeared within 30 minutes after sunflower seed ingestion in all patients. Two patients reported routes of reaction other than ingestion, including cutaneous contact (patient number 8) and inhalation (patient number 7).

Figure 2 shows the classification of the reactions according to the WAO Systemic Allergic Reaction Grading System [23].

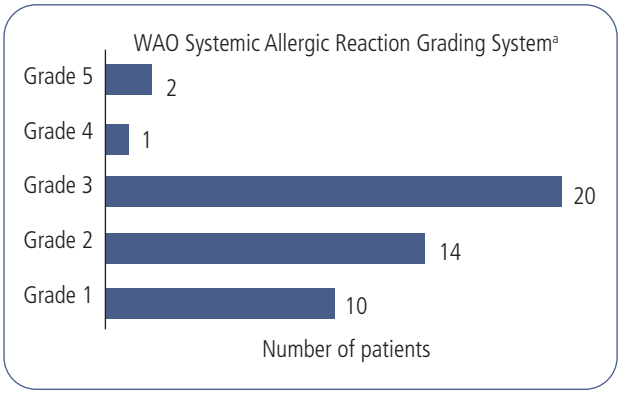

Figure 2. Severity of symptoms according to the World Allergy Organization (WAO) Systemic Allergic Reaction Grading System in 47 patients with sunflower seed allergy.
[a]WAO Systemic Allergic Reaction Grading System. Grade 1, Symptom(s)/sign(s) from 1 organ or system (cutaneous, lips, upper respiratory, throat-clearing, cough not related to bronchospasm, conjunctival, nausea); Grade 2, Previous symptom(s)/sign(s) from ≥2 organs; Grade 3, Lower airways (mild bronchospasm) and/or gastrointestinal and/or uterine cramps; Grade 4, Lower airways (severe bronchospasm) and/or upper airway (laryngeal edema with stridor); Grade 5, Respiratory failure and/or collapse/hypotension and/or loss of consciousness.
In patients with more than 1 reaction to sunflower seed, the most severe reaction was considered.

Table 2. Variability of Symptoms After Sunflower Seed Exposure in 10 Patients Allergic to Sunflower Seed With Multiple Reactions

Patient	Grade of symptoms	
No.	Mildest reaction	Most severe reaction
4	OAS	OAS + urticaria + respiratory + gastrointestinal
6	OAS	OAS + hands swelling + respiratory
7	OAS	OAS + urticaria + gastrointestinal + nasal + conjunctival
10	Urticaria	Urticaria + facial swelling + respiratory
20	OAS + urticaria + swelling	OAS + urticaria + facial swelling + respiratory + collapse
21	Gastrointestinal	Gastrointestinal + urticaria
27	OAS	OAS + urticaria
29	OAS	OAS + respiratory
30	OAS	OAS + respiratory
38	OAS	OAS + foot and hands swelling

Abbreviation: OAS, oral allergy syndrome.

Twenty-three of the 47 patients (49%) reported severe or life-threatening reactions (grade 3 or higher), including bronchospasm, laryngeal edema, gastrointestinal symptoms, syncope, or hypotension. Emergency medical services were requested for 18 patients (38%), and 4 patients (8%) received epinephrine.

Sixteen patients reported more than 1 reaction to sunflower seed before the diagnosis. Of these, 10 (62%) reported different clinical profiles of reactions on each exposure. Table 2 shows the variability of symptoms in the reactions of the 10 patients.

Other Allergies and Comorbidities

A history of rhinitis, asthma, or atopic dermatitis was documented in 41 patients (87%). Forty-three patients (91%) had a history of other food reactions. No significant differences were found for history of atopy or other food reactions according to the age of onset of sunflower seed allergy (younger or older than 18 years).

Sunflower seed was the first food allergy reported in 16 patients. Most patients with sunflower seed allergy had a history of other food allergies preceding the first reaction to sunflower seed (31 patients; 66%). The most frequent food allergies preceding the diagnosis of sunflower seed allergy were those caused by peach (34%), followed by peanut (30%) and nuts (mainly walnut 25%, hazelnut 19%, almond 17%, and pistachio 11%). Other fruits and nuts were involved in <10% of cases.

A reaction to a different seed was reported in 1 patient (patient number 28), who experienced facial swelling after mustard seed ingestion before the diagnosis of sunflower seed allergy.

Skin Tests and Specific IgE Measurements

All patients had a positive result in the sunflower seed SPT (median diameter, 8 mm) or specific IgE (median IgE, 1.1 kU_A/L). Specific IgE values for sunflower seed in patients with a history of atopy (rhinitis, asthma, or atopic dermatitis) significantly exceeded those found in patients with no history of atopy (1.50 [0.56-2.88] kU_A/L vs 0.33 [0.11-0.50] kU_A/L; P=.017).

Patients who were clinically reactive to sunflower seed underwent skin tests and specific IgE testing with the panallergens nsLTP (rPru p 3, rAra h 9, rJug r 3, rCor a 8), profilin (rPru p 4) and 2S albumins (rAra h 2, rJug r 1), as well as other foods according to their history of reactions. There were no significant differences in sensitization to panallergens for age of onset of sunflower seed allergy (younger or older than 18 years). Sensitization to nsLTPs was observed in 26 out of 35 (74%) patients who underwent determination of nsLTP-specific IgE (rPru p 3, rAra h 9, rJug r 3, rCor a 8) and Pru p 3 skin tests (Table 3). Levels of sunflower seed IgE were strongly correlated with levels of IgE to LTPs (Spearman, 0.61-0.83; P<.001). No significant correlation was found between the severity of reactions to sunflower seed and the grade of sensitization to sunflower seed or any food proteins.

Discussion

We studied 47 consecutive adult patients with sunflower seed allergy from a tertiary hospital in Spain to better characterize and improve our understanding of this allergy in adults.

Most patients were characterized by an adult-onset reaction to sunflower seed preceded by a history of atopy (including atopic dermatitis, allergic rhinitis, and asthma) and other food allergies. Onset of symptoms was earlier in patients who

Table 3. Sensitization to Food Proteins and Correlation Between Sunflower Seed IgE, Food Protein Specific IgE, and Severity of Reactions to Sunflower Seed in 47 Patients With Sunflower Seed Allergy.

			Spearman correlation coefficient	
	No. (%) of patients sensitized	Median IgE, kU_A/L	Correlation between SS specific IgE and other proteins specific IgE	Correlation between severity of SS reactions (WAO) and specific IgE (SS and other proteins)
Sunflower seed	47	1.10		
LTPs				
Pru p 3 (peach)	22/26 (85%)	6.7	0.6095 (*P*<.001)	0.1003 (NS)
Ara h 9 (peanut)	22/30 (73%)	1.9	0.8162 (*P*<.001)	0.2702 (NS)
Jug r 3 (walnut)	21/28 (75%)	1.4	0.8319 (*P*<.001)	0.2508 (NS)
Cor a 8 (hazelnut)	15/26 (58%)	0.6	0.7619 (*P*<.001)	0.3255 (NS)
Any LTP (IgE/SPT)	26/35 (74%)			
Other proteins				
Pru p 4 (peach)	4/13 (31%)	0	0.2901 (NS)	0.2665 (NS)
Ara h 2 (peanut)	0/26 (0%)	0	0.5007 (*P*=.009)	0.1207 (NS)
Jug r 1 (walnut)	2/27 (7%)	0	–0.1039 (NS)	0.1117 (NS)

Abbreviations: LTP, lipid transfer proteins; NS, nonsignificant; SS, sunflower seed; WAO, World Allergy Organization.

reported sunflower seed allergy as their first food reaction. The difference in the age of onset could be explained by the sensitization mechanism, with cross-reacting allergens shared by foods and between inhalants and foods being the most frequent in adults [2,24]. However, in our sample, no significant differences were found between the age groups in history of atopy or food allergy or sensitization to panallergens.

Almost half of the patients (49%) experienced severe or potentially life-threatening reactions after sunflower seed ingestion. Few patients underwent oral food challenges with sunflower seed to corroborate the diagnosis owing to the severity of the reactions (confirmed by specific sensitization) and the patients' preference to avoid sunflower seed ingestion.

Other case reports of anaphylactic reactions to sunflower seed have been published [1,8-21]. Garcia Ortiz et al [12] reported 15 reactions to sunflower seed ranging from oral allergy syndrome (OAS) to anaphylaxis in 11 patients from a series of 84 patients monosensitized to *Artemisia* pollen. The authors found a lower proportion of severe reactions, with only 2 cases of anaphylaxis after sunflower seed ingestion. Our results support that sunflower seed allergy should be considered a potential cause of life-threatening reactions.

The high prevalence of systemic reactions in other common food triggers of severe reactions, such as peanuts or nuts, is usually explained by sensitization to stable proteins, such as 2S albumins and nsLTPs [2]. We found no significant correlation between the severity of reactions to sunflower seed and the sensitization to nsLTPs or 2S albumins of other foods. Sunflower seed–specific component-resolved diagnostics could help us predict the severity of specific sensitization patterns.

Among the 16 patients with more than 1 reaction to sunflower seed before the diagnosis, we found that 10 (62%) with a history of OAS experienced more severe reactions to sunflower seed. There are several reports of food-induced systemic reactions in patients with OAS. A nationwide study of pollen food allergy syndrome in Korea [25] reported a prevalence of anaphylaxis of 8.9% in patients with OAS. Skypala [26] associated the variability in clinical presentations of food allergy to atmospheric conditions, with increasing pollen counts and pollution leading to more severe reactions to foods in patients with OAS. Considering our results, strict avoidance of sunflower seed ingestion seems recommendable in sunflower seed–allergic patients, regardless of the severity of the initial reaction.

Despite the high number of severe reactions in our series, many were undertreated, with only 17% receiving epinephrine. Our results are consistent with those of other studies, which routinely report underuse of epinephrine, even though it is the first-line treatment for anaphylaxis [27-29]. A national registry of anaphylaxis in Portugal, including seeds as elicitors of 3% of the reactions, showed that only 43% of patients admitted to the emergency department received epinephrine [28]. Another prospective study of anaphylaxis in an emergency care setting in Denmark reported that epinephrine was administered to only 25% of patients with anaphylaxis [29]. These findings emphasize the need to train both patients and physicians in the treatment of anaphylaxis.

Only 1 of the 47 patients reacted to other seeds (facial swelling after mustard seed ingestion confirmed by specific sensitization). In vitro experiments have demonstrated serological cross-reactivity between sunflower seed and mustard 2S albumins [30], although there are few data in the literature concerning clinically relevant cross-sensitization between different seeds. According to our results, a diagnosis of seed allergy to one seed does not seem to predict allergy to other seeds.

Most patients with sunflower seed allergy had a history of other food allergies preceding the first reaction to sunflower seed, mostly to peach, peanut, and nuts (walnut, hazelnut,

almond, and pistachio). In addition, most were sensitized to nsLTPs from peach, peanut, or nuts, while few patients were sensitized to 2S albumins. Levels of sunflower seed IgE were strongly correlated with levels of IgE to those nsLTPs. Nevertheless, no significant differences were found in the severity of the reactions according to sensitization to nsLTPs. In recent decades, nsLTPs have been identified as sunflower seed allergens, along with other proteins such as profilins and 2S albumins [31-32]. Considering the high prevalence of sensitization to nsLTPs in our area, it remains to be seen whether sensitization to those nsLTPs develops independently or whether cosensitization occurs due to cross-reactivity with allergenic sunflower seed proteins. The literature contains few data on cross-reactivity between sunflower seeds and other foods, with most reported data being for nuts. Cross-reactivity between sunflower seed and pistachio has been demonstrated by inhibition studies [33]. Kortt et al [34] also reported 34% identity between sunflower seed and Brazil nut 2S protein.

With sunflower seed potentially able to cause severe reactions, further research is needed to investigate its allergenic content, determine clinical cross-reactivity between seeds and other foods, and develop component-resolved diagnostics for both diagnosis and prediction of severity associated with specific sensitization patterns.

In summary, most of the reactions to sunflower seed were adult-onset and were preceded by a history of atopy and other food reactions, mainly peach, peanut, and nuts. Sunflower seed reactions are often undertreated, and severity may vary on repeated exposures in the same patient, ranging from OAS to anaphylaxis. Consequently, allergic patients should strictly avoid this food, and an epinephrine autoinjector should be prescribed where indicated.

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Conflicts of Interest

The authors declare that they have no conflicts of interests.

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