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Anaphylaxis in a food allergy outpatient department: one-year review

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KEY WORDS

adults; anaphylaxis; cofactors; food allergy; pediatric

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Summary

Background. Anaphylaxis is an acute, potentially fatal, multi-organ allergic reaction. Our aim was to characterize the population with food induced anaphylaxis followed over a one-year period. **Methods.** Retrospective analysis of clinical files of patients with food anaphylaxis observed in our food allergy consultation during 2016. **Results.** Sixty-two patients were included. In the pediatric group, the implicated allergens were cow's milk, egg and fish and in the adults' group, the commonest allergens were nuts and wheat. Allergy to shrimp affected equally children and adults. The most frequent symptoms were urticaria (85.5%), angioedema (64.5%) and dyspnea (62.9%). Cofactors were present in 32.6% of patients, mainly exercise. Asthma and/or rhinitis were the most frequent comorbidities. **Conclusion.** In accordance to other studies, milk and egg were the most implicated allergens in children. Anaphylaxis in adults reflects the Mediterranean sensitization pattern. Exercise was the most relevant cofactor.

Introduction

Food allergy is an adverse reaction to foods in which immunologic mechanisms have been demonstrated (1), whether IgE-mediated, non-IgE-mediated, or involving a combination of IgE- and non-IgE-mediated mechanisms. It can result in life threatening reactions and has a significant impact on quality of life (2). In the last decades, the prevalence of food allergies has increased in several regions throughout the world (3). Although food allergy is not as prevalent as other allergic diseases, its repercussions on dietary habits and social interaction is quite relevant (4). Allergic reactions to foods are the leading cause of anaphylaxis in patients of all ages outside the hospital setting (5); however, the precise risk of anaphylaxis is unknown (2). Recent data shows an increase in emergency department visits and admissions for food-induced anaphylaxis (5). Although all foods,

theoretically, can induce anaphylaxis, only a restricted number of foods are responsible for the majority of the reactions (3).

Because the severity of allergic reactions to foods cannot be predicted either by the severity of prior reactions or by allergy test results, appropriate recognition of signs and symptoms and prompt initiation of treatment are necessary for optimal outcomes (5).

Incomplete recognition of the signs and symptoms of anaphylaxis can be life-threatening to the patient (5). Allergy testing is quite relevant to determine the cause of anaphylaxis and therefore prevent further reactions. Specialized counseling in a food allergy outpatient is very important, and can be highly efficient. It is important to identify which allergen is responsible for the reaction, and this investigation can include skin testing, specific IgE (sIgE) determination and/or oral food challenges (OFC)

(3,6). The identification of molecular allergens involved can help determine the severity of reaction and relevant cross-reactivities (7).

Food allergy prevalence varies considerably between studies, but is estimated to affect up to 10% of children and 2-3% of adults (2). One European systematic review on the epidemiology of anaphylaxis lists foods as one of the most common causes (8). In Portugal, Gaspar et al, in their study on the frequency of pediatric anaphylaxis, obtained an 84% prevalence of food-induced anaphylaxis (9). Asero et al, in 1100 food-allergic patients, obtained a 5% incidence of food-related anaphylaxis in patients diagnosed with food allergy, over a one year period (10). Two Australian cohorts studies performed in 2001/2002 and 2005/2006, reported seafood, fish and peanut as the most frequently accountable food groups (11). In children, peanuts and tree nuts were the most frequently identified in several studies, but milk, egg and shrimp were also commonly documented (12).

Admission rates for anaphylaxis differ between countries (11). In the USA, food induced anaphylaxis is the leading cause of anaphylaxis treated in emergency departments (ED) (13). Moreover, an upward trend was noticed in the United Kingdom, Italy and New Zealand (11,13).

It is unclear why the highest rates of food-anaphylaxis predominate in children under 5 years of age. Possible reasons include high prevalence of food allergy in this age group, and the possibility that severe reactions are more common before a correct diagnosis is made (2).

Fatalities are more commonly seen in young adults (14), but have a very low incidence rate in preschool years (2). Most importantly, 30% of fatal anaphylaxis cases are triggered by food allergens (5).

The aim of this study is to characterize the population with food induced anaphylaxis followed in our food allergy outpatient department over a one-year period.

Methods

Medical record review

We reviewed the medical records of all patients evaluated in the Food Allergy outpatient of the Allergy and Clinical Immunology Department at Coimbra University Hospital, from January to December 2016. Those with a diagnosis compatible with anaphylaxis in any period of their lives, were selected to be part of the study. Patients of all age groups were included, and were categorized into clusters according to age and culprit food for the first anaphylactic episode. Although some of them later displayed allergic symptoms with other foods, these culprits were excluded from this study.

The clusters were: cow's milk, egg, meat, fish, shellfish, wheat, fresh fruits, tree nuts, peanut and mushroom.

Since the study was retrospective, and based on routine investigations performed on patients spontaneously presenting at the hospital for suspected food allergy, no institutional ethical permission was needed.

Data collection

Physician investigators reviewed 358 medical records of food-allergic patients followed in the food allergy outpatient department (FAOD) of Coimbra's University Hospital.

Exclusion criteria included absence of anaphylaxis clinical criteria, missing data (records lacking documentation of signs and symptoms of anaphylaxis) or loss of follow-up.

All patients with symptoms suggestive of food anaphylaxis were further investigated with skin and/or in vitro testing. Oral food challenges (OFC) to confirm allergy or tolerance were performed in selected cases.

Results were gathered to evaluate demographic data, culprit food, presenting symptoms, treatment options and the presence of atopy. Date of the first anaphylactic event, reported by the patient, was documented.

Anaphylaxis was defined according to the Anaphylaxis guidelines from the European Academy of Allergy and Clinical Immunology (EAACI) (15).

Atopy was defined according to the World Allergy Organization (WAO) (16) and EAACI (12) guidelines. Atopic comorbidities were evaluated and registered in our study population.

Cofactors such as exercise, intake of alcohol and drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs) and angiotensin converting enzyme inhibitors (ACEI) were documented, and were defined according to the EAACI guidelines (1).

Statistical analysis

The results are presented in absolute and relative frequencies. Quantitative variables with normal distribution are expressed as mean \pm standard deviation. Variables not normally distributed are expressed as median (IQR).

Results

From a total of 358 patients observed in the food allergy outpatient department during 2016, 62 patients (17.3%) met criteria for anaphylaxis. Demographic data are summarized in **table I**.

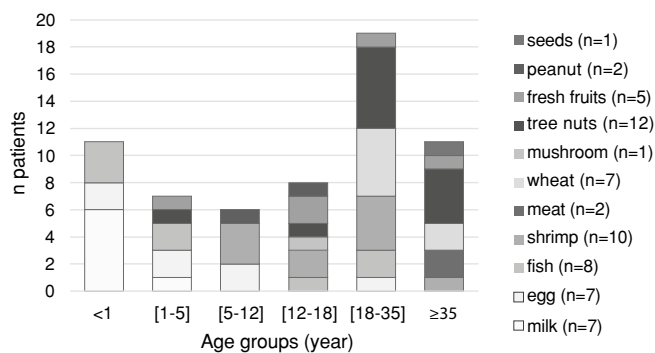
Culprit foods involved in anaphylaxis

The foods implicated in anaphylaxis according to the age of the first episode are specified in **figure 1**. Tree nuts (n = 12), shrimp

Table I - Demographic characteristics of the study participants.

Characteristic	Children n = 32 (51.6%)	Adults n = 30 (48.4%)	No. of patients n = 62
Male	18 (56.3%)	17 (56.7%)	35 (56.5%)
Atopic comorbidities	25 (78%)	22 (73%)	47 (75.8%)
AA	1 (3.1%)	4 (13.3%)	5 (8.1%)
AR	2 (6.2%)	11 (36.7%)	13 (21%)
AA + AR + AD	5 (15.6%)	1 (3.3%)	6 (9.7%)
AA + AR	12 (37.5%)	6 (20%)	18 (29%)
AR + AD	5 (15.6%)	0	5 (8.1%)

Abbreviations: AA, allergic asthma; AR, allergic rhinitis; AD, atopic dermatitis.

Figure 1 - Causes of food-induced anaphylaxis according to the age of the first reaction.

(n = 10) and fish (n = 8) were the most common causes of anaphylaxis in our population. **Table II** summarizes the prevalence of all culprit foods and **table III** showcases demographic and clinical data for the most common causative foods.

Important differences exist in the presentation and etiology of food anaphylaxis between adults and children. Therefore, we analyzed the two populations separately.

Pediatric population

Cow's milk was the most frequent cause of food anaphylaxis in this population (n = 7), and the highest incidence in children below 1 year of age (n = 5). The earliest report of anaphylaxis to milk was in a 15-day newborn boy.

Table II - Triggers of anaphylaxis.

Cause	No. (%) of patients (n = 62)	No. (%) of adults (n = 30)	No. (%) of children (n = 32)
tree nuts (walnut 4, hazelnut 4, almond 1, chestnut 1, pistachio 1, cashew 1)	12 (19.4%)	10 (33.3%)	2 (6.3%)
shrimp (n = 10)	10 (16.1%)	5 (16.7%)	5 (15.6%)
fish (codfish 3, salmon 3, whitefish 1, redfish 1)	8 (12.9%)	2 (6.7%)	6 (18.8%)
milk (cow's milk 7)	7 (11.3%)	0	7 (21.9%)
egg (whole egg 4, raw egg white 1, cooked egg white 1, Bird-egg syndrome 1)	7 (11.3%)	1 (3.3%)	6 (18.8%)
wheat (n = 7)	7 (11.3%)	7 (23.3%)	0
fresh fruits (peach 3, apple 1, kiwi 1)	5 (8.1%)	2 (6.7%)	3 (9.4%)
meat (pork 2)	2 (3.2%)	2 (6.7%)	0
peanut (n = 2)	2 (3.2%)	0	2 (6.3%)
mushroom (n = 1)	1 (1.6%)	0	1 (3.1%)
seeds (sunflower seeds 1)	1 (1.6%)	1 (3.3%)	0

Table III - Culprit foods: comparison by the most common food causes. (IQR - Interquartile range).

Cause	Age, median (IQR), y	Total IgE median (\pm SD), kU/L	No. of patients (%) with atopic comorbidities
Total	21.3 (0.08 - 66.0)	304 (\pm 446.7)	47 (75.8%)
tree nuts	32.2 (2.0 - 62.0)	389.5 (\pm 278.1)	11 (17.7%)
shrimp	24.4 (6 - 66)	602 (\pm 553.9)	10 (16.1%)
fish	9.1 (0.48 - 30)	646.5 (\pm 533.2)	5 (8%)
milk	1.6 (0 - 10)	219 (\pm 232.1)	6 (9.7%)
egg	6.4 (0.72 - 20)	638 (\pm 567.9)	6 (9.7%)
wheat	37.8 (20 - 64)	404.9 (\pm 263)	3 (4.8%)

Six patients (85.7%) had no previous diagnosis of allergy to cow's milk protein (CMP) before the anaphylactic episode. Of those, the anaphylactic reaction occurred in 4 children after the first intake of adapted milk formula (between 15 days and 2 months of age), all with previous exclusive breastfeeding, and in 2 patients after the intake of puree containing milk, both at 6 month-old.

Only one patient had a first episode of anaphylaxis to milk occurring after the first year of life. This 10 year-old boy had a known diagnosis of allergy to CMP, and the episode of anaphylaxis occurred after an accidental ingestion of food with trace amounts of milk. He later developed symptoms of allergy to shrimp (oral allergy syndrome and urticaria) in adulthood, but never had an episode of anaphylaxis to this food. Another patient allergic to milk also presented allergic symptoms with the ingestion of cow's meat and fruits from the *Rosacea* family. This patient was sensitized to Bos d 6, but not to *Rosacea* fruits lipid transfer protein (LTP). Four patients (57.1%) underwent an OFC with milk, all positive. Three patients had an immediate reaction in the OFC but one had a late reaction (abdominal cramps and diarrhea). Of those, only one patient underwent an oral tolerance induction protocol (at 15 years old) which drastically diminished the number of accidental reactions. All the patients kept follow-up until adulthood, and none of them acquired natural tolerance to milk.

Among the 6 children with anaphylaxis to egg, three were already known to have egg allergy before the anaphylactic episode. All of these patients had egg allergy symptoms since the first year of life, and the anaphylactic episode occurred with food containing egg as an occult allergen. The anaphylaxis was the first symptom of egg allergy in two patients (33.3%), and were elicited by cooked egg yolk on the first attempt to introduce egg in the diet. All reactions were IgE-mediated, with all patients having positive specific IgE (sIgE) to egg yolk, egg white, ovomucoid (Gal d 1) and ovalbumin (Gal d 2).

Of the 6 patients with anaphylaxis to egg, 3 are in absolute egg avoidance, 2 are in avoidance of raw egg and 1 tolerates extensively cooked egg. None of the patients underwent tolerance induction protocols, due to the severity of the egg allergy.

Five patients (83.3%) had atopic comorbidities.

The third most frequent cause of anaphylaxis in our pediatric population was fish, in 6 patients (18.8%). In the pediatric population, all the anaphylaxis to fish occurred in the first year of life with the introduction of this food in the infant diet. Codfish was the most common cause (60%), but red fish and salmon were also implicated. All reactions were IgE mediated, with positive skin prick tests (SPT) and sIgE. OFC with alternative fish were performed in all patients, and two challenges were positive (codfish and mackerel). During follow-up, 2 patients are in strict avoidance of all fishes, 2 patients only tolerate tuna, and 2 patients acquired tolerance to fish and now have no food restrictions.

The episodes triggered by shrimp ($n = 5$) were more frequent in school-age children and adolescents (6 to 14 years). All reactions were IgE mediated, and all patients presented sensitization to multiple shellfish. Eighty percent of the patients ($n = 4$) were sensitized to shrimp tropomyosin, Pen a 1. Four patients presented symptoms of rhinitis related with house dust mite exposure and had positive specific IgE to mite tropomyosin, Der p 10. All the patients are in strict avoidance of shellfish.

Peanut was the culprit food in only two patients. Both patients had symptoms with the ingestion of tree nuts and fresh fruits and were sensitized to peach LTP, Pru p 3. None of them tolerates peanut.

The anaphylaxis due to kiwi was in a 4 year-old boy; he had positive prick-test and sIgE to kiwi, but none of the kiwi's molecular components were searched. This patient also presented positive sIgE to peach LTP and profilin, despite he never had complaints with the ingestion of any *Rosacea* fruits.

The patient with anaphylaxis due to mushroom was a 17 year-old boy who developed symptoms during a handball game in

hot and humid environment, after a meal containing meat and mushrooms cooked with wine. He had a personal history of allergic rhinitis. The patient had positive prick-to-prick test to *Agaricus bisporus* (the mushroom ingested), and positive prick test and sIgE to *Alternaria alternata* fungus. The cross-reactivity between *A. bisporus* and *A. alternata* was confirmed by SDS-PAGE Immunoblotting and Immunoblotting-inhibition assays. The patient underwent sublingual immunotherapy with *A. alternata* extract for 5 years which alleviated the allergic rhinitis symptoms, and he never had other systemic reaction to foods. Nowadays, the patient is in mushroom restriction.

Adult population

In our sample, anaphylaxis due to tree nuts was the most frequent cause of food anaphylaxis in the adult population ($n = 10$), and its frequency was higher in young adults (18 to 35 years). Of those patients, two had symptoms with the ingestion of fresh fruits and were sensitized to Pru p 3; two were sensitized to both Pru p 3 and wheat LTP, Tri a 14. One of the patients sensitized to both Pru p 3 and Tri a 4 had symptoms related to multiple cofactor-mediated food reactions to different groups of foods.

The second most frequent cause of anaphylaxis in the adult population was wheat; it was the culprit food in 7 patients (23.3%). All the reactions were wheat-dependent exercise induced anaphylaxis (WDEIA), and all patients tolerated wheat when eaten without exercise. In three patients, non-steroidal anti-inflammatory drugs (NSAIDs) were also cofactors. All patients presented sensitization to other flours namely: maize ($n = 6$), rye ($n = 5$) and barley ($n = 3$). Four patients (57%) were sensitized to ω -5-gliadin and 2 (28.6%) to wheat LTP, Tri a 14. Only 2 patients were atopic. None of the patients had symptoms with other foods.

Shrimp was the culprit food in five (16.7%) patients. Sixty percent of patients with allergy to shrimp were sensitized to Pen a 1. Only one patient had a cofactor-mediated reaction and it was due to the intake of ACEI drugs and alcohol. All patients were atopic.

One case of anaphylaxis due to egg was registered in a 20 year-old woman, with history of bird-egg syndrome. The anaphylaxis was the first manifestation of egg allergy.

Two patients had anaphylaxis to meat (a male and a female), and both were sensitized to galactose-alpha-1,3-galactose (alpha-gal). In regards to risk factors to meat allergy, both of them denied ever being bitten by thicks, but the male spent his childhood in Africa and the female was a farmer.

Anaphylaxis due to fish ($n = 2$), fresh fruits ($n = 2$) and sunflower seeds ($n = 1$) were also reported in the adult population.

Tables IV and **V** summarize the molecular components identified in the pediatric and adult population, and respective sIgE results.

Table IV - Pediatric population: molecular components identified and respective mean sIgE.

Molecular component	No. children sensitized	sIgE Mean (\pm SD), kU/L
Bos d 4	7	7.03 (\pm 12.9)
Bos d 5	7	9.53 (\pm 8.9)
Gal d 1	6	5.09 (\pm 12.1)
Gal d 2	6	8.88 (\pm 7.97)
Pen a 1	4	15.06 (\pm 34.7)
Gad c 1	4	2.09 (\pm 2.3)
Pru p 3	2	0.67 (\pm 1.9)

Table V - Adult population: molecular components identified and respective mean sIgE.

Molecular component	No. adults sensitized	sIgE Mean (\pm SD), kU/L
Pru p 3	4	29.15 (\pm 33.7)
Tri a 19	4	7.74 (\pm 9.02)
Tri a 14	4	10.05 (\pm 8.28)
Pen a 1	3	6.22 (\pm 55.23)
Gad c 1	2	0.63 (\pm 0.22)
Galactose-alpha-1,3-galactose (alpha-gal)	2	4.34 (\pm 1.17)

Signs and symptoms of anaphylaxis

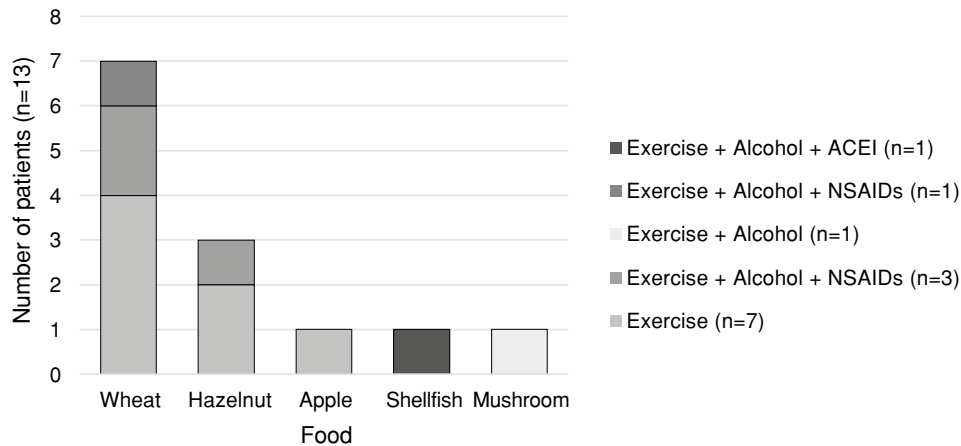
Of the 62 patients who experienced anaphylaxis, 87.1% and 70.1% reported urticaria and angioedema, respectively. Shortness of breath (66.1%) was the second most frequent complaint, followed by laryngeal involvement (45.2%). **Table VI** summarizes the frequency of signs and symptoms of anaphylaxis according to the age group.

Emergency department attendance and treatment

Fifty-five patients (88.7%) resorted to the ED due to anaphylaxis symptoms. However, of the patients observed in the ED, only 18 (29%) were treated with epinephrine. From these, 15 (83%) had cardiovascular events, glottic edema or syncope / presyncope. The anaphylactic episodes related to the ingestion of tree nuts ($n = 12$) were the ones where epinephrine was more frequently administered ($n = 5$), followed by wheat-dependent

Table VI - Signs and symptoms of associated to anaphylaxis.

Sign or symptom	No. (%) of children (n = 32)	No. (%) of adults (n = 30)	Total (%) of patients (n = 62)
urticaria	27 (84.4%)	27 (90%)	54 (87.1%)
angioedema	21 (65.6%)	23 (76.7%)	44 (70.1%)
shortness of breath	20 (62.5%)	21 (70%)	41 (66.1%)
laryngeal involvement	9 (28.1%)	19 (63.3%)	28 (45.2%)
vomiting	16 (53.3%)	1 (3.3%)	20 (32.3%)
oral pruritus	8 (25%)	4 (13.3%)	12 (19.6%)
rhino-conjunctivitis	3 (9.4%)	7 (23.3%)	10 (16.1%)
syncope or presyncope	2 (6.3%)	6 (20%)	8 (12.9%)
hypotension	3 (9.4%)	6 (20%)	9 (14.5%)
diarrhea and/or abdominal cramps	1 (3.1%)	2 (6.7%)	3 (4.8%)
dysphagia	0	1 (3.3%)	1 (1.6%)

Figure 2 - Cofactor mediated reactions according to culprit food.

exercise induced anaphylaxis (n = 4) and shrimp-related anaphylaxis (n = 4). There were no differences in the use of epinephrine in patients with or without asthma.

Acute treatment of anaphylaxis also included antihistamines (58%), corticosteroids (47%), and bronchodilators (3%).

Of the patients observed in the ED (n = 55), only one had measurement of serum tryptase during the episode.

Cofactors and anaphylaxis

Thirteen patients (21%) had cofactor-mediated anaphylaxis. Cofactor mediated reactions according to culprit food are shown in **figure 2**.

Exercise was the most frequently implied cofactor followed by alcohol. Six patients had more than one cofactor, being exercise and alcohol the most common combination.

All anaphylaxis associated to wheat were exercise induced. Hazelnut was the second most frequent cause of food dependent exercise induced anaphylaxis (FDEIA).

Most of the FDEIA occurred in adults (n = 11); there were only 2 cases in the pediatric population, 2 male adolescents with exercise mediated reactions to apple and mushroom.

Discussion

The studies on the incidence and characteristics of food-induced anaphylaxis in both children and adults are few. There are some

studies that focus on the incidence of all causes of anaphylaxis in the Portuguese population (9,17,18), most of them concentrate on the pediatric population. Regarding the prevalence of food allergy in the Portuguese population only a handful of studies are available, and report prevalences of about 1% in the adult population (1) and 8.5% in the paediatric population (14). A study on self-reported food allergies, via telephone call, in a small sample of adults from the city of Oporto obtained a prevalence of 5.2% (12).

In an Italian study that analysed the prevalence of adult food anaphylaxis in 19 allergy outpatient clinics, they obtained a prevalence of 5% in a one-year period (10). A study that evaluated the incidence of anaphylaxis in a pediatric emergency department in Madrid cited that food was the most frequently suspected trigger of anaphylaxis, with a prevalence of 68% of children admitted with anaphylaxis (19). In a Boston cohort study with 1115 pediatric patients on the prevalence of food-related acute allergic reactions, authors concluded that in a 6-year period the annual number of visits for food-related acute allergic reactions increased from 164 to 391, with approximately half of these cases with criteria for food-induced anaphylaxis (20).

Perhaps due to the higher incidence of food allergy and, consequently, food anaphylaxis in children, there are more studies on the prevalence and characteristics of food anaphylaxis in this age group than in adults.

The prevalence of food anaphylaxis in our sample was 17.3%, which is higher than in most of previous studies. This could be due to the fact that our patients were taken from a consultation where most of the patients already had a diagnosis of food allergy, which can be a bias in our study. However, the prevalence of anaphylaxis can vary according to geographical and cultural factors.

The male preponderance (56.5%) in food-induced anaphylaxis presentations noted in this study is not consistent with other published studies that cited a slightly higher incidence in females (8,9,10,21).

So far, most studies in this field were done in English-speaking countries with dietary habits that are different from the Portuguese population.

In the pediatric population, the most common causes of anaphylaxis were milk (21.9%), egg (18.8%) and fish (18.8%). When compared with the results from English or American studies our results are quite different, as in English-speaking countries the most frequent causes are peanut, tree nuts, fish and milk (12,13,14,22). However, when compared with studies in European countries, especially in Mediterranean countries like Italy and Spain, the results are quite similar (milk, egg and tree nuts). This could be due to cultural differences, as peanut and peanut-derived products (e.g. peanut butter) is scarcely consumed in Portugal, whereas fish is a widely consumed food

by the Portuguese population, and is introduced into the infant diet usually before 9 months of age, even when there is an atopic risk. The fact that roasted peanuts are more consumed in Portugal than peanut butter may contribute to the lower incidence of peanut allergy. There are some studies showing that the way peanuts are processed may profoundly influence the sensitization process (23). The high prevalence of sensitization to cow's milk and eggs, even before their introduction into the infant diet, could be owed to a possible sensitization during fetal life or after birth, through breast milk (24). Peanut anaphylaxis was listed in 2 patients (6.3%).

Among the adult population, tree nuts (33.3%), wheat (23.3%) and shrimp (16.7%) were the more commonly implicated foods. These results are more similar to those found in English-speaking countries, where reactions due to tree nuts, fish and shellfish are the most prevalent (20). Nevertheless, as in children, our results are comparable to those of the Mediterranean countries, where reactions due to LTP sensitization are frequent (10). Twenty percent of anaphylaxis occurred in patients sensitized to LTP.

All cases of wheat anaphylaxis were WDEIA. Of those, most patients (57.1%) were sensitized to ω -5-gliadin, which is coherent with previous studies that described this protein as the major allergen of immediate wheat allergy and WDEIA (7,23).

As previously reported by studies of food allergy prevalence in European countries, in our patients the types of foods most frequently implicated are included in the so-called "big eight allergens": milk, egg, peanut, tree nuts, wheat, soy, fish and shellfish (4). However, and as Lozoya-Ibáñez et al reported in their work about self-reported food allergy, the individual prevalence of each food type is distinct, which may be due to cultural differences in food habits. As in their study, our results may be due to the lower size of our sample in comparison with the other studies in this area.

Cutaneous (urticarial and/or angioedema) symptoms were the most common clinical manifestations, as has been previously described (4), followed by respiratory tract symptoms and gastrointestinal symptoms (19).

The mainstay of treatment of any kind of anaphylactic reaction is the timely administration of epinephrine. Epinephrine was administered in 29% of the patients, which is consistent with previous reports, describing a 25-44% administration rate (13). Tree nuts and wheat were the most common triggers in the epinephrine treated reactions; and we found no difference in the administration in patients with or without asthma.

Other therapies including H1-antihistamine, corticosteroids, bronchodilators, oxygen and fluid support are considered second- and third-line therapies (10). Systemic antihistamines are commonly used in anaphylaxis but have only been demonstrated to relieve cutaneous symptoms (10). Corticosteroids are not ef-

fective for the treatment of acute anaphylaxis, but may have a role in preventing or ameliorating biphasic or protracted anaphylaxis, which may occur in up to 20% of anaphylactic episodes (5).

Although these therapeutics ameliorate the symptoms of anaphylaxis, their use alone is not recommended in the treatment of the reaction (10).

Conclusions

Anaphylaxis is still an under-recognized and under-treated disease. Food anaphylaxis is a medical emergency which occurs unpredictably. It causes distressing symptoms to the individual, family and caregivers due to its potential to cause a fatal reaction. Unfortunately, in many situations epinephrine is not administered as the first line therapy, which can be dramatic in a severe episode.

Although allergy tests results correlate with the risk of reactivity to foods, they do not correlate with the severity of reactions. Thus, all physicians should be aware that any patient with food allergy is at risk of anaphylaxis at some point in their lives, and should inform them of the risks of their disease and how to deal with a severe reaction.

Our study is a contribution to the study of food allergies and anaphylaxis in Portugal and may be useful in comparison with other studies carried out in other countries.

Conflict of interest

The authors declare that they have no conflict of interest.

References

- Muraro A, Werfel T, Hoffmann-Sommergruber K, et al. EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. *Allergy Eur J Allergy Clin Immunol* 2014; 69(8):1008-25.
- Umasunthar T, Leonardi-Bee J, Turner PJ, et al. Incidence of food anaphylaxis in people with food allergy: A systematic review and meta-analysis. *Clin Exp Allergy* 2015; 45(11):1621-36.
- Burks AW, Tang M, Sicherer S, et al. ICON: Food allergy. *J Allergy Clin Immunol* [Internet] 2012; 129(4):906-20. Available from: <http://dx.doi.org/10.1016/j.jaci.2012.02.001>
- Lozoya-Ibáñez C, Morgado-Nunes S, Rodrigues A, Lobo C, Taborda-Barata L. Prevalence and clinical features of adverse food reactions in Portuguese adults. *Allergy, Asthma Clin Immunol* [Internet] 2016; 12(1):36. Available from: <http://aacijournal.biomed-central.com/articles/10.1186/s13223-016-0139-8>
- Wang J, Young MC, Nowak-Węgrzyn A. International survey of knowledge of food-induced anaphylaxis. *Pediatr Allergy Immunol* 2014; 25(7):644-50.
- Moore LE, Stewart PH, deShazo RD. Food allergy: what we know now. *Am J Med Sci* 2017; 353(4):353-66.
- Cardona V, Ansotegui IJ. Component-resolved diagnosis in anaphylaxis. *Curr Opin Allergy Clin Immunol* [Internet] 2016; 16(3):244-9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26945180>
- Liew WK, Williamson E, Tang MLK. Anaphylaxis fatalities and admissions in Australia. *J Allergy Clin Immunol* [Internet] 2009; 123(2):434-42. Available from: <http://dx.doi.org/10.1016/j.jaci.2008.10.049>
- Gaspar Á, Santos N, Piedade S, et al. One-year survey of pediatric anaphylaxis in an allergy department. *Eur Ann Allergy Clin Immunol* 2015; 47:197-205.
- Asero R, Antonicelli L, Arena A, et al. Causes of food-induced anaphylaxis in Italian adults: a multi-centre study. *Int Arch Allergy Immunol* 2009; 150(3):271-7.
- Koplin JJ, Mills ENC, Allen KJ. Epidemiology of food allergy and food-induced anaphylaxis: is there really a Western world epidemic? *Curr Opin Allergy Clin Immunol* 2015; 15(5):409-16.
- Falcão H, Lunet N, Lopes C, Barros H. Food hypersensitivity in Portuguese adults. *Eur J Clin Nutr* 2004; 58:1621-5.
- Amaral R, Morais-Almeida M, Gaspar Á, Sa-Sousa A, Martins H, Fonseca J. Anaphylaxis in Portugal: First registries of the Portuguese Catalog of Allergies and Other Adverse Reactions. *Rev Port Imunoalergologia* 2014; 22(1):23-32.
- Bento M, Armando F, César-Ramos J. Epidemiology of food allergy in Portugal. *Pediatr Pulmonol* 2001; 23:38-40.
- Muraro A, Roberts G, Worm M, et al. Anaphylaxis: Guidelines from the European Academy of Allergy and Clinical Immunology. *Allergy Eur J Allergy Clin Immunol* 2014; 69(8):1026-45.
- Simons FER, Arduso LRF, Dimov V, et al. World allergy organization anaphylaxis guidelines: 2013 update of the evidence base. *Int Arch Allergy Immunol* [Internet] 2013; 162(3):193-204. Available from: <http://dx.doi.org/10.1186/s40413-015-0080-1>
- Alvarez-Perea A, Ameiro B, Morales C, et al. Anaphylaxis in the Pediatric Emergency Department: analysis of 133 Cases After an Allergy Workup. *J Allergy Clin Immunol Pract* 2016;1-8.
- Rudders SA, Banerji A, Vassallo MF, Clark S, Camargo CA. Trends in pediatric emergency department visits for food-induced anaphylaxis. *J Allergy Clin Immunol* 2010; 126(2):385-8.
- Yu JE, Lin RY. The Epidemiology of Anaphylaxis. *Clin Rev Allergy Immunol* [Internet] 2015; Available from: <http://link.springer.com/10.1007/s12016-015-8503-x>
- Järvinen KM. Food-induced anaphylaxis. *Curr Opin Allergy Clin Immunol* [Internet] 2011; 11(3):255-61. Available from: <http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landing-page&an=00130832-201106000-00017>
- Kool B. Adult food induced anaphylaxis hospital presentations in New Zealand. *Postgrad Med J* 2016; 90(1068):2747.
- Mondoulet L, Paty E, Drumare MF, et al. Influence of thermal processing on the allergenicity of peanut proteins. *J Agric Food Chem* 2005; 53(11):4547-53.
- Scherf KA, Brockow K, Biedermann T, Koehler P, Wieser H. Wheat-dependent exercise-induced anaphylaxis. *Clin Exp Allergy* 2016; 46(1):10-20.
- Panesar SS, Javad S, De Silva D, et al. The epidemiology of anaphylaxis in Europe: A systematic review. *Allergy Eur J Allergy Clin Immunol* 2013; 68(11):1353-61.