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One-year survey of paediatric anaphylaxis in an allergy department

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Summary

Aim. To determine the frequency of anaphylaxis in an allergy outpatient department, allowing a better understanding regarding aetiology, clinical manifestations and management, in children and adolescents. **Methods.** From among 3646 patients up to 18 years old observed during one-year period, we included those with history of anaphylaxis reported by allergists. **Results.** Sixty-four children had history of anaphylaxis (prevalence of 1.8%), with mean age 8.1 ± 5.5 years, 61% being male. Median age of the first anaphylactic episode was 3 years (1 month - 17 years). The majority of patients had food-induced anaphylaxis (84%): milk 22, egg 7, peanut 6, tree nuts 6, fresh fruits 6, crustaceans 4, fish 4 and wheat 2. Food-associated exercise-induced anaphylaxis was reported in 2 adolescents. Drug-induced anaphylaxis occurred in 8%: 4 non-steroidal anti-inflammatory drugs and 1 amoxicillin. Three children had cold-induced anaphylaxis, one adolescent had anaphylaxis to latex and one child had anaphylaxis to insect sting. The majority (73%) had no previous diagnosis of the etiologic factor. Symptoms reported were mainly mucocutaneous (94%) and respiratory (84%), followed by gastrointestinal (42%) and cardiovascular (25%). Fifty-one patients were admitted to the emergency department, although only 33% were treated with epinephrine. Recurrence of anaphylaxis occurred in 26 patients (3 or more episodes in 14). **Conclusions.** In our paediatric population, the main triggering agent of anaphylaxis was IgE-mediated food allergy. Epinephrine is underused, as reported by others. Often, children have several episodes before being assessed by an allergist. We stress the importance of systematic notification and improvement of educational programmes in order to achieve a better preventive and therapeutic management of this life-threatening entity.

Introduction

According to the World Allergy Organization (WAO) (1), anaphylaxis is defined as an acute, multi-organ system, potentially life-threatening hypersensitivity reaction caused by the release of chemical mediators from mast cells and basophils. It can be triggered by immune mechanisms (allergic anaphylaxis) mediated by immunoglobulin E (IgE) (allergic IgE-mediated anaphylaxis) or other immune mechanisms (non-IgE-mediated allergic anaphylaxis) or non-immunologic mechanisms (non-allergic anaphylaxis).

It is a clinical emergency, being the most severe form of allergic disease. A practical and clinically based criteria definition, irrespective of the underlying mechanisms, that would allow the easy recognition of anaphylaxis both at the hospital and at the clinic levels, was one of the main objectives of a multidisciplinary symposium sought to standardize the diagnostic approach and treatment of this entity (2,3).

In 2006, Sampson *et al.* (4) revised and published the criteria for the diagnosis of anaphylaxis that included, in addition to the mucocutaneous, cardiovascular and respiratory symptoms,

Appendix 1 - Clinical criteria for the diagnosis of anaphylaxis (Adapted from Sampson *et al.*)⁴.

Anaphylaxis is highly likely when any one of the following three criteria is fulfilled:

1. Sudden onset of an illness (minutes to several hours) with **involvement of the skin, mucosal tissue or both** (e.g. generalized hives, itching or flushing, swollen lips-tongue-uvula) **and at least one of the following**:
 - a. **Sudden respiratory compromise** (e.g. dyspnea, wheeze-bronchospasm, stridor, reduced FEV₁/ PEF, hypoxemia)
 - b. **Sudden reduced BP or associated symptoms** of end-organ dysfunction (e.g. hypotonia-collapse, syncope, incontinence)
2. **Two or more of the following**, that occur suddenly after exposure **to a likely allergen or other trigger for that patient** (minutes to several hours):
 - a. Sudden skin or mucosal symptoms and signs (e.g. generalized hives, itching or flushing, swollen lips-tongue-uvula)
 - b. Sudden respiratory symptoms and signs (e.g. dyspnea, wheeze-bronchospasm, stridor, reduced FEV₁/ PEF, hypoxemia)
 - c. Sudden reduced BP or symptoms of end-organ dysfunction (e.g. hypotonia-collapse, syncope, incontinence)
 - d. Sudden gastrointestinal symptoms (e.g. crampy abdominal pain, vomiting)
3. **Reduced BP after exposure to a known allergen** for that patient (minutes to several hours):
 - a. Infants and children: low systolic BP (age-specific) or greater than 30% decrease in systolic BP¹

FEV₁: Forced expiratory volume in 1 second; PEF: Peak expiratory flow; BP: Blood pressure.

¹Low systolic blood pressure for children is defined as less than 70 mmHg from 1 month to 1 year, less than [70 mmHg + (2x age)] from 1 to 10 years, and less than 90 mmHg from 11 to 17 years.

gastrointestinal symptoms when occurring upon the exposure to a likely allergen or trigger, allowing the standardization of the definition of anaphylaxis. These criteria, initially proposed by the American Academy of Allergy, Asthma & Immunology (AAAAI), were later accepted by the European Academy of Allergy and Clinical Immunology (EAACI) (5) and the WAO (6). The prevalence of anaphylaxis during life is estimated to be from 0.05 to 2% (7), with a recent review of European studies pointing to an estimated prevalence of 0.3%, meaning that 1 in every 300 persons suffers an episode of anaphylaxis during their lifetime (8).

The incidence of anaphylaxis was estimated at between 8.4 per 100 000 persons/year in population studies in the UK (9) to 50 individuals per 100 000/year in the United States (10) with a mortality of 1 to 3 cases per million inhabitants/year (11).

There has been an increase in the prevalence of anaphylaxis over time, especially in paediatric age groups (8,11,12) and an increase in the number of hospital admissions for anaphylaxis in preschool children (8,12-15), being food the most often implicated cause of anaphylaxis in this age group (8,11,15,16).

In Portugal, the prevalence or incidence of anaphylaxis in the general population are not known to date. A study performed by Morais-Almeida *et al.* in 2006 reported a prevalence of 1.3% of anaphylaxis in patients observed at an outpatient allergy clinic for one year, half of them belonging to the paediatric age group (17).

Aim

The aim of this study was to contribute to a better knowledge of the epidemiology of anaphylaxis, based on the voluntary notifi-

cation by allergy specialists, in order to estimate the prevalence of anaphylaxis in the paediatric age groups in a specialized allergy department, over a one year period, and identify the main clinical manifestations and etiological agents of anaphylaxis in these children and adolescents.

Material and methods

Population

A systematic reporting of anaphylaxis was implemented in the allergy department of CUF Descobertas Hospital from the 1st of January to the 31st of December 2011. All allergists (twelve) of the department were invited to participate in the study and a meeting was organized in order to promote the voluntary notification of all observed cases. All accepted to participate and joined this study. Episodes of anaphylaxis occurring in children and adolescents under 18 years old followed at the outpatient clinic of our department, described by the patient or caregiver, were reported.

During the one-year period 3646 patients aged less than 18 years old were observed, having been included all children with episodes fulfilling criteria of severe anaphylaxis. The diagnosis of anaphylaxis was made when "at least one episode of severe systemic reaction" occurred, as defined by the consensus, when in the presence of at least one of the three clinical criteria outlined in the **appendix 1** (4). A questionnaire with demographic and clinical data was completed. Etiological investigation was conducted by the attending allergy specialist

using appropriate diagnostic tests in each case, including skin tests with the suspected etiologic agent and/or assays of serum specific IgE, or other methods such as ice cube testing when appropriate.

Questionnaire

A questionnaire was carried out by the allergist to all patients with history of anaphylaxis in order to characterize the following parameters:

- Demographics, including age, gender and place of residence;
- Family history of allergic disease;
- Personal history of asthma or other allergic disease;
- Date of the first anaphylactic reaction and detailed description of the clinical manifestations: mucocutaneous, respiratory, gastrointestinal and cardiovascular; elapsed time between exposure to the causal factor and the onset of symptoms; description of the performed treatment, including information about the use of epinephrine; place of anaphylaxis occurrence; attendance to the emergency department and hospitalization;
- Previous prescription and use of a self-injectable epinephrine from an auto-injector device;
- Number of episodes of anaphylaxis, reproducibility and reasons for recurrence;
- Characterization of the causative factor involved and the date of diagnosis; in case of a previous diagnosis, assessment of the context of exposure: accidental contact or challenge test.

Etiological investigation

The skin prick tests with the suspected allergen(s) (food allergens, latex, antibiotics or hymenoptera venom) were performed on the anterior surface of the forearm with a minimum distance of 2 cm between each allergen extract and using metal lancets applied perpendicularly to the skin with a 1 mm penetration (PrickLancet®, Stallergenes, Antony, France), taking into account the recommended eviction timings for medications and using standard methodology (18,19). Histamine hydrochloride 10 mg/mL was used as a positive control and a solution of 0.5% phenol as a negative control. The reading was performed after 15 minutes. Tests with a mean wheal diameter ≥ 3 mm were considered positive. In patients with suspected food allergy, skin prick tests with the food were performed whenever the test with the allergenic extract was negative or unavailable. For suspected allergy to antibiotics and hymenoptera venom, prick and intradermal tests were performed according to international guidelines (20,21), after obtaining informed consent and at least six weeks after the anaphylactic reaction.

When available, the assay for specific IgE (sIgE) was performed through the UniCAP® method to the suspected allergen (Ther-

mo Fisher Scientific, Uppsala, Sweden). Results were considered positive for sIgE ≥ 0.35 kU/L.

The ice cube test was performed by applying a cold stimulus (0 to 4°C) on the anterior surface of the forearm by a sequential time of 3, 5, 10 and 20 minutes to obtain a positive response (wheal). This test was considered negative if a wheal did not appear after 20 minutes of exposure (22).

Atopy

Atopy was defined as positive test for at least one allergen from a panel of aeroallergens (Bial-Aristegui® extracts, Bilbao, Spain) adapted according to the age of the patient: mites (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Blomia tropicalis* and *Lepidoglyphus destructor*), pollens (grass mix, *Parietaria judaica*, *Artemisia vulgaris*, *Plantago lanceolata*, *Olea europaea*, *Cupressus spp* and *Platanus spp*), fungi (*Alternaria alternata*), dog and cat dander.

Statistical analysis

The results are presented as absolute and relative frequencies. Quantitative variables with normal distribution are expressed as mean \pm standard deviation. Variables not normally distributed are expressed as median (minimum-maximum). The Chi-square test and calculation of odds ratios with confidence interval of 95% was used to test association between qualitative variables and considered significant for a p-value < 0.05 .

Results

Over the one year period, 64 patients were reported with history of anaphylaxis (prevalence of 1.8%), with a mean age (standard deviation (SD)) of 8.1 ± 5.5 years and a median of 7 years (5 months to 17 years old) at the time of observation, including 19 adolescents (aged 12 years or older); 39 (61%) were male.

Atopy, personal and family history of allergic disease is presented in **table 1**. Only two children had no personal or family history of allergic disease. The majority (91%) had personal history of allergic disease, and 44% had asthma as co-morbidity.

The median age of the first anaphylaxis episode was of 3 years (1 month to 17 years old). In 14 children (22%) the first episode occurred in the first year of life and in 50 (78%) up to 5 years of age. Only 6 (9%) had the first episode in adolescence.

Clinical manifestations

Reported symptoms are shown in **figure 1**. In 51 patients (80%) both skin and respiratory symptoms occurred. Four children aged 1 to 2 years did not have mucocutaneous manifestations. The number of respiratory symptoms was similar in patients

Table 1 - Frequency of atopy and personal and family history of allergic disease.

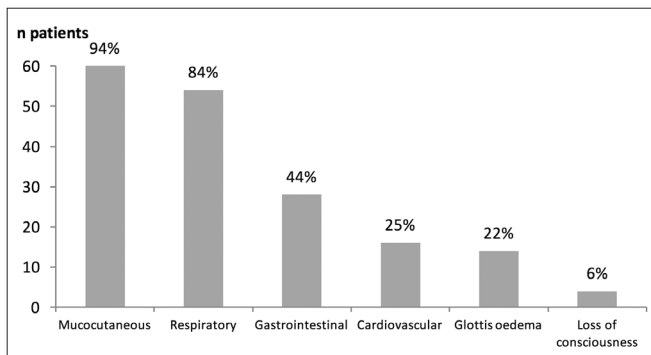
	n	(%)
Atopy	44	(75)¹
Personal history of allergic disease	58	(91)
Rhinitis	47	(73)
Eczema	37	(58)
Asthma	28	(44)
Food allergy	14	(22)
Family history of allergic disease	50	(78)

¹Percentage of children on whom skin prick tests with aeroallergens were performed (n = 59).

with and without asthma (84% vs. 83%, $p = 1000$). In all cases with gastrointestinal complaints, food was the suspected etiological agent, and in 25 (89%) cases it occurred in children aged less than 3 years. Cardiovascular manifestations, glottis oedema or loss of consciousness occurred in 25 patients (39%); the diagnosis of asthma was not a risk factor for these symptoms ($p = 0.114$).

The majority (86%) of the reactions started within 30 minutes after exposure to the etiological agent. The 5 delayed reactions began after 2 to 3 hours of exposure and included 4 children aged less than 2 years with food-induced anaphylaxis and a 3 year-old boy with insect sting anaphylaxis.

Figure 1 - Number and percentage of patients according to clinical manifestations at the first episode of anaphylaxis.



Emergency department attendance and treatment

Thirty-six (57%) of the first episodes of anaphylaxis occurred at home, 11 (17%) in restaurants, 11 (17%) on vacation or recreational sites, 4 (6%) at the hospital and 2 (3%) at school.

Fifty-one patients (80%) resorted to the emergency department. However, only 21 (33%) were treated with epinephrine; from these, 13 (62%) had cardiovascular events, glottis oedema or loss of consciousness. Three (5%) patients were hospitalized for more than 24 hours with no need of mechanical ventilation and there were no fatalities. There were no differences in the use of the emergency department or epinephrine administration in patients with and without asthma ($p = 0.872$ and $p = 0.331$, respectively).

Previous diagnosis, recurrence and use of self-injectable epinephrine

Seventeen patients (27%) had a prior diagnosis of allergy: in 15 children, anaphylaxis occurred after accidental contact with the causative agent and in 2 during an oral food challenge with cow's milk. In 47 patients (73%) the diagnosis of allergy was performed after the episode of anaphylaxis. Epinephrine for self-administration was prescribed to all but 6 children, who could maintain complete evicition (anaphylaxis to drugs) or who weighed less than 7.5 kg.

In 26 patients (41%) anaphylaxis occurred more than once: 12 patients with 2 episodes, 9 with 3 to 4 episodes and 5 patients with 5 or more episodes. Three patients had successfully used the self-injectable epinephrine from an auto-injector device.

Etiological study

In 54 patients (84%) anaphylaxis was food-induced. The remaining causes are specified in **table 2**. Two adolescents had more than one cause of anaphylaxis, accounting for a total of 66 reports of etiological agents: anaphylaxis to shrimp and acetylsalicylic acid (ASA), and anaphylaxis to cow's milk with subsequent food dependent exercise-induced anaphylaxis (FDEIA).

The foods implicated in anaphylaxis according to the age at the first episode are specified in **figure 2** and the results of further study in **table 3**. Three children had anaphylaxis with two different food groups (fish, peanut or milk associated with anaphylaxis to egg).

Milk was the most frequent cause of food anaphylaxis, with the highest incidence in children below 2 years of age. Eight of the 10 children with anaphylaxis to milk in the first year of life had no previous diagnosis of milk allergy, while 11 of the 12 children older than one year had a previous diagnosis of allergy to cow's milk proteins (CMP), with 82% of the first episodes of anaphylaxis in this age group occurring in the context of accidental ingestion: food with trace amounts of milk in restaurants and at school; dairy products, such as yogurt, butter and cheese; milk-containing cookies and bread. A 5 year-old child diagnosed with allergy to CMP had anaphylaxis after goat milk ingestion at home by rec-

Table 2 - Causes and patients' characteristics of non food-induced anaphylaxis.

Etiological agent	Age ¹	Sex	Atopy	Complementary study
Drug-induced anaphylaxis (n = 5)				
NSAID: paracetamol	8 years	M	Yes	negative sIgE, SPT, ID and CAST
ibuprofen	3 years	M	Yes	n.p.
ibuprofen	5 years	F	No	n.p.
ASA	16 years	F	Yes	n.p.
Amoxicillin	3 years	F	Yes	sIgE MDM = 0.13kU/L; positive ID ²
Cold-induced anaphylaxis (n = 3)				
Cold drink	14 years	F	Yes	positive ICT at 10 minutes
Plunge in the sea	14 years	M	Yes	positive ICT at 3 minutes
Plunge in the sea	2 years	F	No	positive ICT at 3 minutes
FDEIA (n = 2)				
Soy and green bean	11 years	M	Yes	positive SPT to soy and green bean
Cow's milk	17 years	M	Yes	positive SPT and sIgE to cow's milk, alpha-lactalbumin, beta-lactoglobulin and casein ³
Latex allergy (n = 1)				
Peri-operative, chestnut and kiwi	6 years	F	Yes	Positive SPT to latex, chestnut and kiwi; positive sIgE to latex, rHev b 1, rHev b 3, rHev b 5, rHev b 6.01 and rHev b 6.02 ⁴
Allergy to insect sting (n = 1)				
Mosquito (3 reproducible reactions)	3 years	M	Yes	negative sIgE to mosquito

¹Age at the first reaction.

²Second anaphylaxis episode during the intradermal test with amoxicillin (2.5 mg/mL), performed after negative skin prick tests to amoxicillin, PPL, MDM and penicillin G.

³Adolescent who underwent oral tolerance induction to cow's milk and tolerates cow's milk at rest.

⁴Patient with history of 22 surgeries for spina bifida and latex-fruit syndrome, currently under sublingual latex immunotherapy.

M: male; F: female; NSAID: non-steroidal anti-inflammatory drug; ASA: acetylsalicylic acid; SPT: skin prick tests; ID: intradermal tests; sIgE: specific immunoglobulin E; CAST: cellular antigenic stimulation test; n.p.: not performed; MDM: penicillin allergens (*minor* determinants); ICT: ice cube test; FDEIA: food-dependent exercise-induced anaphylaxis.

ommendation of a non-allergist doctor. In those eight children with anaphylaxis to milk in the first year of life who had no previous diagnosis of milk allergy, the anaphylactic reaction occurred: after the first intake of milk-containing puree (between 4 to 6 months age) in 4; after the first intake of adapted milk formula (between 4 to 11 months age) in 3 (2 with previous exclusive breastfeeding and 1 with previous partially hydrolysed formula); and 1 one-month-old hospitalized child after adopted milk formula intake.

At the time of the study, children with CMP anaphylaxis had a median age of 8 years (5 months to 17 years old). Thirteen (59%) underwent an oral tolerance induction protocol, which was effective in all cases, with current tolerance of 200 ml of

cow's milk per day and the possibility of free diet. In these children submitted to oral tolerance induction the median milk-specific IgE level at the time of diagnosis was of 25.8 kU/L (1.43 to > 100 kU/L).

Of children with anaphylaxis to egg, only one had a previous diagnosis of allergy. Of the 7 children, 3 (43%) acquired natural tolerance to the whole egg, 2 children aged 4 and 6 years are in absolute egg avoidance and 2 children aged 2 and 6 years are avoiding egg white while tolerating egg yolk.

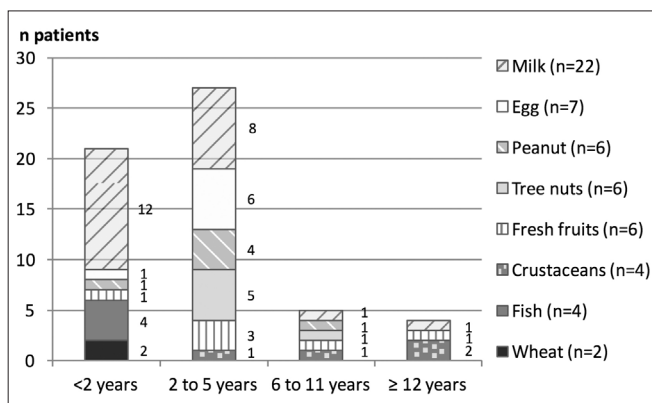
Of the total of patients studied, 53 (83%) were concluded to have had an IgE-mediated reaction, corresponding to 51 (94%) of patients with food-induced anaphylaxis.

Table 3 - Foods implied in food-induced anaphylaxis.

Food	Age at the first reaction ¹	IgE-mediated n (%)	
Milk (41%) (cow's milk 21, goat's milk 1)	1 year (1 month - 15 years)	21	(95%)
Egg (13%) (whole egg 4, raw egg 2, egg white 1)	3 years (10 months - 4 years)	7	(100%)
Peanut (11%) (n = 6)	4 years (10 months - 6 years)	6	(100%)
Tree nuts (11%) (pine nut 2, walnut 2, cashew 1, hazelnut 1)	3 years (2-6 years)	6	(100%)
Fresh fruit (11%) (apple 1, banana 1, kiwi 1, melon 1, papaya 1, pineapple 1)	4 years (1-17 years)	5	(83%) ²
Crustaceans (7%) (shrimp 3, barnacle 1)	11 years (5-16 years)	4	(100%)
Fish (7%) (n = 4)	1 year	2	(50%)
Wheat (4%) (n = 2)	6 months	2	(100%)

¹Median (minimum-maximum).

²Skin prick test (with the extract and the fresh fruit) and specific IgE negative to kiwi.

Figure 2 - Causes of food-induced anaphylaxis according to the age at the first reaction

Discussion

This study, conducted in an outpatient allergy department, confirms IgE-mediated food allergy as the leading cause of anaphylaxis in children, accounting for more than three-quarters of reported cases. Other identified causes were drug allergy (anti-inflammatory and beta-lactam antibiotics), cold, exercise, latex and insect bite.

Compared to the study by Morais-Almeida *et al.* (17), performed with a similar methodology and duration, we observed an increase in the prevalence of anaphylaxis from 1.3% to 1.8% over a 5-year interval. Bearing in mind that notification was based on voluntary participation, it is admissible that some cases may not have been reported, thus, any deviation from our estimation will be by default.

Regarding the causes of anaphylaxis, the results are in agreement with previous studies conducted in outpatient allergy clinics in Portugal (17,23) and in a paediatric emergency department in Australia (16). In these studies, the main causes of anaphylaxis were foods in 71 to 85%, drugs in 6 to 11%, and insects in 3 to 6%. In children hospitalized for anaphylaxis in Israel (24), foods were also the most frequent cause (43%), although allergy to drugs (22%) and to insect venom (14%) were more frequent. In the anaphylaxis survey carried out by the Latin American Society of Asthma, Allergy and Immunology (SLAAI), by applying the OLASA survey (Online Latin American Survey of Anaphylaxis) in children, the foods were also the most frequent cause, although with a higher reported frequency for drugs (28%) and insect sting (26%) allergy (25).

Among foods, milk was the most often implicated cause of anaphylaxis, as reported in previous studies (43-53%) (16,17,23),

being more frequent in the first years of life (24). According to Silva *et al.* (23), milk was the causative food in 47% of children with food anaphylaxis, followed by fish and shellfish (23%), cereals and nuts (14%) and egg (9%). According to Morais-Almeida *et al.* (17), the implicated food was milk in 53% of children under the age of 15, fish in 19%, egg in 14%, crustaceans in 14%, peanut in 6%, fresh fruits in 6% and tree nuts in 3%. In the present study, we observed an increased frequency of anaphylaxis to peanut and tree nuts (11% each), with an approximation to the values found in the Australian study (18% to peanut and 17% for tree nuts) (16).

We underline the absence of anaphylaxis episodes during allergen immunotherapy protocols, confirming the good current safety of this treatment (26).

We also emphasize that, in the current study, it was possible to conclude the cause of anaphylaxis in all patients, in contrast to previous studies, where idiopathic anaphylaxis was reported with a frequency of 5 to 7% of children (16,24). This is probably related to the fact that patients were evaluated in a specialized department and to the greater availability of differentiated means of diagnosis.

The possible occurrence of systemic reactions during the diagnostic procedures, as reported in the child with immediate-onset anaphylaxis induced by intradermal test with amoxicillin (**table 2**), also reinforce the need of referring these patients to specialized centers. These tests must always be performed based on the consensus published by the European Network of Drug Allergy (ENDA)/EAACI (21), beginning with a more diluted concentration. Even though, in this child the intradermal test was accompanied by respiratory and cutaneous systemic symptoms, which was immediately treated with intramuscular epinephrine, followed by anti-histamine and corticosteroid, with total resolution.

Several studies suggest that the diagnosis of asthma is a risk factor for the occurrence of severe, potentially fatal, anaphylactic reactions to food (5,27). One limitation of this study was the fact that reactions were not categorized according to the degree of severity. However, we observed that patients with asthma had no increased frequency of respiratory symptoms or of symptoms considered more severe, such as glottis oedema, cardiovascular symptoms or loss of consciousness, and that there were no differences in attendance to the emergency department or to epinephrine administration. Nonetheless, we were not able to assess the level of asthma control before the episode, which could be the determining factor for more severe anaphylaxis.

Regarding gastrointestinal symptoms, Rudders *et al.* (28) have described that, although uniformly present in all age groups, nausea and vomiting are more common in children, occurring in 53% of children up to 2 years, 34% of preschool aged children, 29% of school aged children and only 17% of adolescents.

In the present study, 89% of gastrointestinal manifestations occurred in children aged less than 3 years, which reinforces the importance of including these symptoms in the diagnostic criteria of anaphylaxis, especially at younger ages. Moreover, the absence of cutaneous symptoms, as occurred in 4 patients, does not exclude the diagnosis of anaphylaxis.

The high frequency of anaphylaxis caused by accidental exposure, in restaurants, recreational activities and at school, starting in the first 30 minutes after contact, as well as the high number of recurrences (17,23,25,29), emphasizes the importance of education of teachers, catering professionals and the general public for the rapid identification and action in this situation. In the present study recurrence of anaphylaxis happened in 41% of cases, with five children having suffered more than 4 episodes. This frequency is similar to that reported in the OLASA survey (42%) (25), but higher to the one observed by Cianferoni *et al.* (29) in a 7-year follow-up survey of children with anaphylaxis. Moreover, the education of patients and caregivers is crucial, for the correct evaluation of the ingredients listed on labels, especially in situations of food allergy with potentially severe reactions that might occur even with trace amounts of the responsible food, such as milk, peanut and tree nuts. All patients and caregivers should be given a document containing the agents to avoid and possible alternatives, as well as the treatment to be carried out in case of accidental contact. The recognition of the signs of anaphylaxis and early and proper use of epinephrine from an auto-injector device should also be reinforced.

Despite epinephrine being recommended as the first-line treatment in anaphylaxis consensus and guidelines (5,6,27,30), and its non-utilization or delayed administration being a risk factor for biphasic, more severe anaphylaxis reactions and death (5,6,31), it remains underused in the emergency department. In our study performed 5 years earlier, the use of epinephrine was reported in 26% of patients, with an increase to 33% in the present study, similar to that reported by Solé *et al.* in the OLASA survey (34.6%) (25), but still falling short in relation to data presented in other countries (72 to 76%) (16,24). This emphasizes the importance of continuing the work started in undergraduate and postgraduate medical education and the incorporation of anaphylaxis diagnosis and treatment protocols in emergency departments. Also, the implementation of digital reports of allergy, with exchangeable information between health facilities, will be important to improve the recognition and treatment of anaphylaxis (32).

In children, there is no absolute contraindication for the administration of epinephrine, although the risk-benefit ratio should be weighed in cases of known cardiac disease (5). Self-injectable epinephrine, currently available in doses of 0.15 mg and 0.30 mg, may be prescribed in children from 7.5 kg, since apparently there is no risk of administering a higher dose than recom-

mended in a healthy child and the availability of an auto-injector epinephrine device can be life-saving (5,27). Education for the patient and caregivers on when and how to use the device is essential.

The occurrence of anaphylaxis can have a profound effect on the quality of life of the children and their family. Finally, we reinforce the importance of an adequate and streamlined referral to allergy specialists in order to improve the correct diagnosis, investigate triggers and cofactors, adopt effective preventive measures such as allergen avoidance, structure a management plan with an emergency action plan, offer alternatives, namely to foods or drugs, and implement a treatment with allergen immunotherapy (hymenoptera venom, latex) or tolerance induction (food, drug) when appropriate. Database networks promoted by scientific societies, such as the Portuguese Society of Allergology and Clinical Immunology (SPAIC), and national reporting systems such as the recently implemented Portuguese Catalog of Allergies and other Adverse Reactions (CPARA) (32) will allow the improvement of knowledge of this disease and to delineate better strategies for prevention and treatment.

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