

ORIGINAL ARTICLE

Improving anaphylaxis management in a pediatric emergency department

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Abstract

Background: The management of anaphylaxis in pediatric emergency units (PEU) is sometimes deficient in terms of diagnosis, treatment, and subsequent follow-up. The aims of this study were to assess the efficiency of an updated protocol to improve medical performance, and to describe the incidence of anaphylaxis and the safety of epinephrine use in a PEU in a tertiary hospital.

Methods: We performed a before–after comparative study with independent samples through review of the clinical histories of children aged < 14 years old diagnosed with anaphylaxis in the PEU according to the criteria of the European Academy of Allergy and Clinical Immunology (EAACI). Two allergists and a pediatrician reviewed the discharge summaries codified according to the International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) as urticaria, acute urticaria, angioedema, anaphylactic shock, unspecified allergy, and anaphylactic shock. Patients were divided into two groups according to the date of implantation of the protocol (2008): group A (2006–2007; the period before the introduction of the protocol) and group B (2008–2009; after the introduction of the protocol). We evaluated the incidence of anaphylaxis, epinephrine administration, prescription of self-injecting epinephrine (SIE), other drugs administered, the percentage of admissions and length of stay in the pediatric emergency observation area (PEOA), referrals to the allergy department, and the safety of epinephrine use.

Results: During the 4 years of the study, 133,591 children were attended in the PEU, 1673 discharge summaries were reviewed, and 64 cases of anaphylaxis were identified. The incidence of anaphylaxis was 4.8 per 10,000 cases/year. After the introduction of the protocol, significant increases were observed in epinephrine administration (27% in group A and 57.6% in group B) ($p = 0.012$), in prescription of SIE (6.7% in group A and 54.5% in group B) ($p = 0.005$) and in the number of admissions to the PEOA ($p = 0.003$) and their duration ($p = 0.005$). Reductions were observed in the use of corticosteroid monotherapy (29% in group A, 3% in group B) ($p = 0.005$), and in patients discharged without follow-up instructions (69% in group A, 22% in group B) ($p = 0.001$). Thirty-three epinephrine doses were administered. Precordial palpitations were observed in one patient.

Conclusion: The application of the anaphylaxis protocol substantially improved the physicians' skills to manage this emergency in the PEU. Epinephrine administration showed no significant adverse effects.

There is no universally accepted definition of anaphylaxis. In 2005, several clinical criteria were proposed by Sampson et al. (1) to aid patient identification. These criteria have been included in some of the most widely used therapeutic guide-

lines (1–4). Study of the distinct features of anaphylaxis is hampered by the various definitions used, the wide variability of clinical presentations, and the absence of a sensitive and specific diagnostic test. Incidence and prevalence rates for

anaphylaxis range between 21.28 and 49.8 per 100,000 persons/year (5, 6).

Epinephrine is the treatment of choice in anaphylaxis, although the grade of evidence supporting the use of this drug is low and based on consensus documents and expert recommendations (7–10). Moreover, epinephrine is scarcely used (11) for several reasons, including fear of its possible adverse effects. Some studies have reported that this drug is used in 15% of patients diagnosed with anaphylactic shock (12), while others have reported figures above 50% (13).

Proper management of children with anaphylaxis does not end at discharge. Some patients may benefit from prescription of self-injectable epinephrine (SIE) devices. Patients should also be instructed in the treatment of new episodes and their prevention. To do this, they should be referred to allergy units and services where the triggering allergen can be identified, the possibility of appropriate etiologic treatment evaluated (14), and the risk of possible new episodes established.

Application of these recommendations is very low (15), even in series reporting the highest figures for epinephrine treatment (13). The percentage of patients referred to an allergist specialist after an anaphylactic reaction varies from 15% to 33%. Some authors have proposed that a multidisciplinary approach involving allergists and other specialists could improve the management of these patients in emergency departments and their follow-up after discharge (16,

17). Educational activities such as seminars have proved to be useful educating caregivers (18). Nevertheless, the efficacy and the implementation of the anaphylaxis guidelines in emergency departments have not been evaluated.

Thus, in 2008, a protocol for the management of children with anaphylaxis in the pediatric emergency unit (PEU) was designed by the pediatrics and allergy departments of our hospital (Fig. 1), according to the EAACI Position Paper (3) to aid the identification and improve the treatment of anaphylactic reactions in the PEU. Two years after its implementation, our main aim was to evaluate its efficiency. To our knowledge, this is the first study performed with this aim.

Secondary aims were to describe the safety of the use of epinephrine in children with anaphylaxis and to analyze the incidence and epidemiological characteristics of these children in our hospital, because data on the epidemiology of anaphylaxis in Spain are limited.

Methods

A before–after comparative study was performed with independent samples in children aged <14 years old attended for anaphylaxis between January 1, 2006, and December 31, 2009, in the PEU of a tertiary hospital.

The management protocol in the PEU was designed jointly by the pediatrics and allergy departments (Fig. 1) according to the EAACI anaphylaxis Position Paper (3), published in

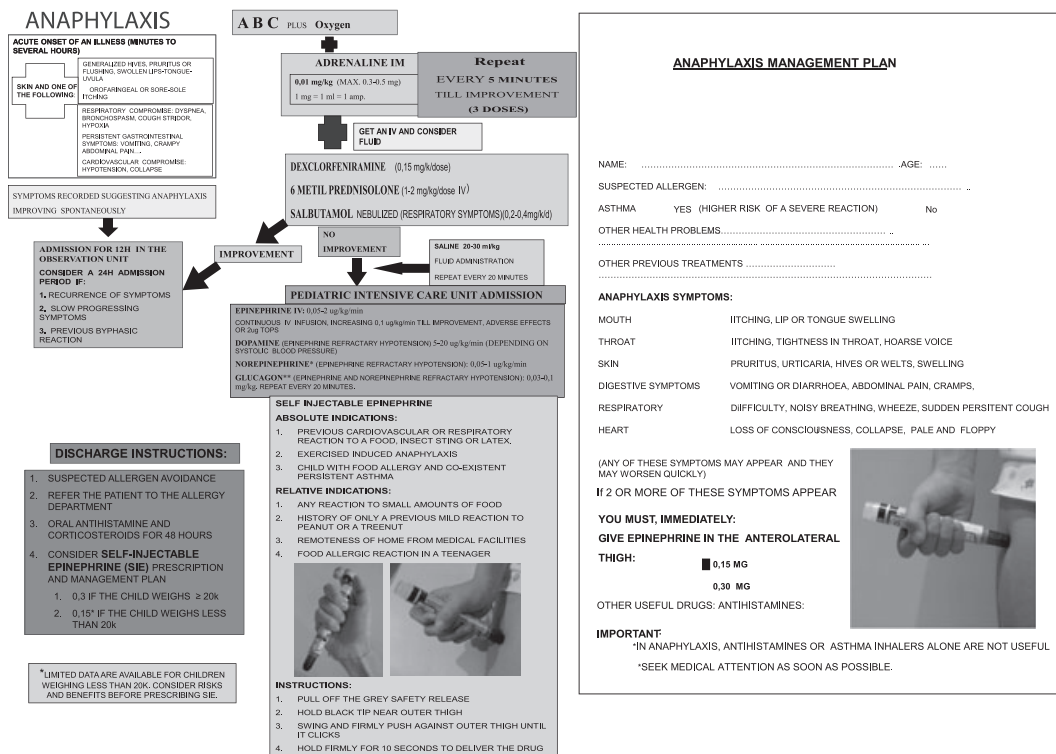


Figure 1 Anaphylaxis management protocol in the Pediatric Emergency Unit. A, Airway control; B, Breath; C, Circulation.

2007. This protocol was presented in a clinical session with resident physicians and the PEU team. The importance of diagnosing patients, early intramuscular epinephrine administration, admission to the pediatric emergency observation area (PEOA) and the importance of prescribing SIE and referring patients to the allergy department at discharge were stressed. This protocol was included in the routine practice of the PEU in January 2008.

All the PEU discharge summaries, codified according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9 CM), described elsewhere were revised. These discharge summaries were divided into two groups, according to the date the protocol was introduced. Group A included all patients attended in 2006 and 2007, and group B all those attended between 2008 and 2009. These reports were always examined separately by two allergists and a pediatrician.

All patients attended in the PEU with the following discharge diagnoses were selected initially: urticaria (708.9), acute urticaria (708.9), angioneurotic edema (995.1), angioedema (995.1), allergy unspecified not elsewhere classified (995.3), and anaphylactic shock (995.0). Discharge summaries providing sufficient written information to meet the criteria for anaphylaxis proposed by Sampson et al. (Table 1) were identified as anaphylaxis and selected for further analysis, but only those identified by the three reviewers were finally included.

Exclusion criteria consisted of discharge summaries not containing sufficient written information to suspect an anaphylaxis, without taking the drug treatment received in the PEU into account, discharge summaries containing clinical data suggestive of other diagnoses and/or those cases not identified by all the reviewers.

Table 1 Clinical criteria for anaphylaxis according to the criteria proposed by Sampson et al. (1)

Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue or both (e.g., generalized hives, pruritus or flushing, swollen lips-tongue-uvula).

1. And at least one of the following:
 - a. Respiratory compromise (e.g., dyspnea, bronchospasm, stridor, hypoxia).
 - b. Cardiovascular compromise (e.g., hypotension, collapse).
2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):
 - a. Involvement of the skin or mucosal tissue (e.g., generalized hives, itch, flushing, swelling).
 - b. Respiratory compromise (e.g., dyspnea, bronchospasm, stridor, hypoxia).
 - c. Cardiovascular compromise (e.g., hypotension, collapse).
 - d. Persistent gastrointestinal symptoms (e.g., crampy abdominal pain, vomiting).

3. Hypotension after exposure to known allergen for that patient (minutes to several hours):

Hypotension for children is defined as systolic blood pressure <70 mmHg from 1 month to 1 year (<70 mmHg + (2 × age)) from 1 to 10 years, and <90 mmHg from 11 to 17 years.

The variables analyzed were as follows: demographic characteristics, clinical manifestations (involvement of distinct organs), a history of atopy and suspected allergen reported by the parents in the clinical history, treatment received in the emergency department, epinephrine administration and its route of administration, the adverse effects observed after epinephrine use, prescription of an SIE in the PEU, admission to the PEOA and length of stay, and referrals to the allergy department after discharge.

For the statistical analysis, the PASW Statistics 18 (2009) (Chicago, EEUU; SPSS, inc.) was used. The Kappa coefficient was used to calculate agreement among the reviewers. Differences in the percentage of symptomatic patients in the PEU, epinephrine administration, prescription of SIE, number of admissions to the PEOA, and the number of patients discharged without follow-up instructions were analyzed using the Chi-square test. Differences among the clinical features and corticosteroid therapy were analyzed using the Fischer test, and the median lengths of stay in the PEOA were assessed through the Mann–Whitney test.

Results

During the study period, 133,591 children were attended in the PEU. A total of 1673 discharge summaries and their codes were identified, and 127 were excluded because of missing information. Five patients were also excluded because of lack of agreement among the reviewers. Sixty-four discharge summaries were identified as cases of anaphylaxis, corresponding to 57 distinct patients. There were 31 discharge summaries in group A and 33 in group B (Fig. 2). The coefficient of agreement (k) among the reviewers was 0.41 [CI (95%): 0.29–0.54].

Fifty-three patients had one episode of anaphylaxis. One patient had four episodes, another had three, and two patients had two episodes during the follow-up. Cases of anaphylaxis represented 3.4% of patients attending the PEU for the diagnoses reviewed. The incidence of anaphylaxis in the PEU was 4.8 new cases per 10,000 patients.

Patient characteristics are detailed in Table 2. The median age was 3 years (range: 0.2–13 years) in group A and 4 years (range: 0.5–13 years) in group B. Skin was the most frequently involved organ, followed by respiratory and gastrointestinal symptoms. Cardiovascular and/or neurological involvements were infrequent. Most patients were symptomatic on arrival at the PEU. The most frequently suspected cause was food, although no trigger could be identified in the clinical history in 21% of cases in both groups.

Drug treatment consisted of epinephrine in 27% of group A and 57.5% of group B patients ($p = 0.012$) and was administered intramuscularly in four patients (40% of the doses) in group A and in 15 patients (65.2% of the doses) in group B. Four patients in group B required more than one epinephrine dose in the PEU.

Thirty-three doses of epinephrine were administered in 27 patients. Only one patient showed adverse effects after the administration of a single dose of intramuscular epinephrine, consisting of palpitations that ceased without specific

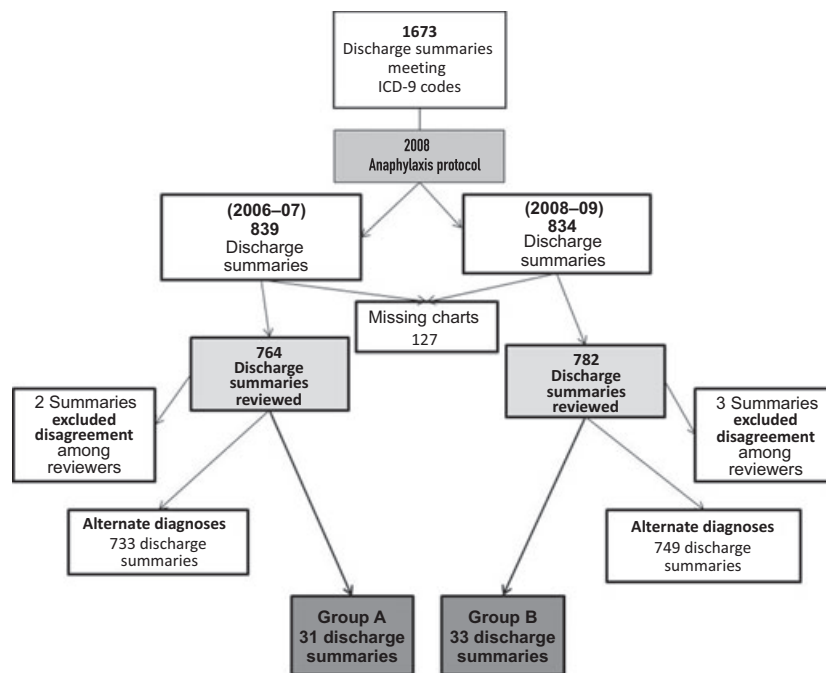


Figure 2 Discharge summaries inclusion procedure. Flowchart.

treatment. All patients received the correct doses according to the protocol.

Analyzing other drugs administered during the episode, nine patients (29%) received corticosteroids exclusively in group A and one patient (3%) in group B ($p = 0.005$). No drug treatment was provided in six patients (20%) in group A and in two patients (6%) in group B ($p = 0.14$).

SIE devices were prescribed in two patients in group A (6.7%) and in 15 (57.5%) in group B ($p < 0.0005$) (Fig. 3).

Fifteen patients (49%) in group A and 28 (84.8%) in group B were admitted to the PEOA ($p = 0.003$). The median length of admission was 2.5 h (range: 0.5–72 h) in group A and was 9 h (range: 0.5–12 h) in group B ($p = 0.003$).

Referrals to the allergy department after discharge were made in three patients (10%) in group A and 12 (38%) in group B (Fig. 4).

Discussion

Therapeutic guidelines are 'systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances' (19), but guidelines alone are not capable of modifying physicians' practice (20). The limitations and problems of anaphylaxis management in the emergency department have been well documented (21), consisting of the following: (i) lack of anaphylaxis symptom recognition, (ii) lack/delay of epinephrine administration, (iii) lack of knowledge regarding SIE and lack of follow-up care instructions. We performed the first study assessing the efficiency of a specific protocol based on current anaphylaxis guidelines. It was centered on symptom recognition, emergency treatment, and subsequent

Table 2 Patients' characteristics

	A group	B group	
Age (Median, IQ)	3 (0.2–13)	4 (0.5–13)	0.1
Sex (V/M)	21/9	15/18	0.09
Clinical manifestations			
Skin	96.7% (30)	97% (32)	1.0
Respiratory	83.3% (25)	69.3% (23)	0.4
Digestive	26.7% (8)	27.3% (12)	0.4
Cardiovascular	10% (3)	3% (1)	0.3
Neurological	– (0)	3% (1)	0.3
Symptomatic at PED arrival	92.9% (29)	78.8% (26)	0.15
Suspected allergen			
Milk	9 (30%)	12 (36.4%)	0.7
Hen egg	3 (10%)	4 (12.1%)	1.0
Nuts, treenuts	5 (16.7%)	4 (12.1%)	0.7
Fish	3 (10%)	1 (3%)	0.3
Legumes	1 (3.3%)	1 (3%)	1.0
Drugs (NSAID)	2 (6.7%)	–	0.2
Unknown	6 (21%)	6 (21%)	1.0
Other foods	1 (3.3%)	5 (15.2%)	0.2
Parentally reported other diagnosis			
No atopy	4 (13.3%)	6 (18.2%)	0.7
Atopic dermatitis	3 (10%)	3 (9.8%)	1.0
Food Allergy	3 (10%)	5 (15.2%)	0.7
Asthma	4 (13.3%)	3 (9.1%)	0.7
Asthma plus FA	11 (36.7%)	10 (30.3%)	0.8
Atopic D plus FA	2 (6.7%)	4 (12.1%)	0.7
FA + AD + Asthma	1 (3.3%)	2 (6.1%)	1.0

PEU, Pediatric Emergency Unit; FA, Food allergy; AD, Atopic Dermatitis.

p values for comparison between Group A and Group B

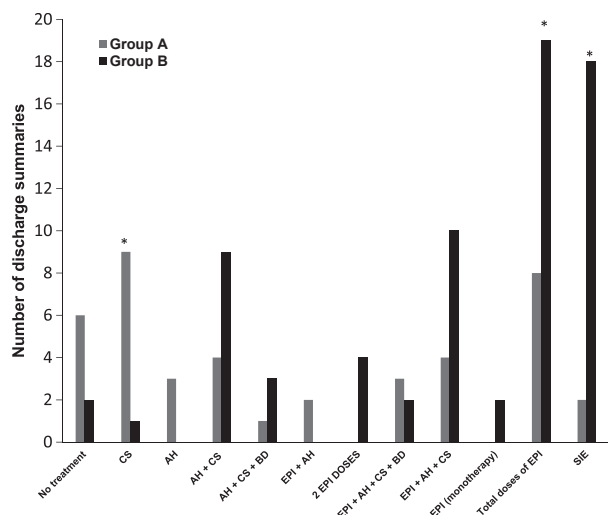


Figure 3 Anaphylaxis treatment in the PEU. AH, antihistamines; CS, corticosteroids; BD, bronchodilator; Epi, epinephrine.*p values < 0.005.

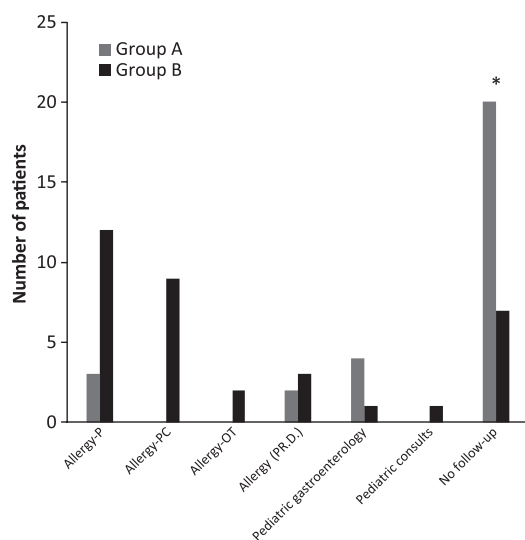


Figure 4 Referrals after discharge. Allergy(P): Referred to Allergy from the PEU. Allergy (PC): Referred to Allergy from Primary Care. Allergy (Ot): Referred to other Allergy Units. Allergy (previously diagnosed): patients previously controlled in the Allergy Department.

follow-up. It was distributed to medical and nursing staff in the PEU, within the hospital's medical continuing formation program. We measured changes in the medical performance and one clinical outcome: the incidence of side effects related to epinephrine use.

The PEU discharge summaries were codified according to the ICD-9-CM. These codes have been frequently used by other authors in patient selection (11, 12, 17). However, the

ICD-9-CM conflates the terms 'anaphylactic reaction' and 'shock'. Some authors have reported that current ICD-9 codes underestimate the number of cases of anaphylaxis (22). Thus, some series have based their results on reviews of patients identified as having anaphylactic shock (995.0) (12), while others have also reviewed related or similar codes such as 'allergy, unspecified (995.3)', 'anaphylactic shock due to adverse food reaction (995.6)', 'venom bite or sting (989.5)' and/or 'urticaria (708)' (11). The latest modifications of the ICD-9 have broadened the heading of 'anaphylactic shock due to adverse food reaction (995.6)', adding distinct codes according to the triggering foods (23) and maintaining the anaphylactic shock code. To include all cases of anaphylaxis, we reviewed not only the code for anaphylactic shock (995.0), but also those for urticaria (708.9), acute urticaria (708.9), angioneurotic edema (995.1), angioedema (995.1), and allergy, unspecified (995.3).

We took into account the possibility of underdiagnosis (24) and that the responsible physician may not have agreed with the code for anaphylactic shock and may have chosen another code, even though treating the patient as if for true anaphylaxis. Therefore, 'cases' of anaphylaxis were identified by the two allergists and the pediatrician, who separately reviewed all the discharge summaries using the criteria of Sampson et al. (1). These criteria have been used in distinct anaphylaxis treatment guidelines but have not been universally accepted (25). The agreement observed (0.41) among the three reviewers was moderate and was considered acceptable considering the number of the reviewers and diagnostic issues, previously addressed. Despite these limitations, we believe that our diagnoses were accurate and reflected the clinical practice of any allergy department.

The incidence of anaphylaxis in our PEU was 4.8 new cases per 10,000 patients attended in the unit. The Hospital Universitario Donostia is a tertiary hospital in San Sebastian with a PEU census of approximately 33,000 patients per year. It is very difficult to compare our data with other pediatric series because of the different age limits used in different countries and the source of the medical data, among other factors. Our sample's median ages were 3 (group A) and 4 years (group B), and other series including children with the same age limits have reported similar data (26), while surveys including children younger than 18 have observed higher incidence rates in teenagers (27). Age and weight differences may have important clinical repercussions in the subsequent follow-up measure indications: A teenager will be able to self-administer a SIE device while a toddler might not receive a prescription and future treatment will rely on caregivers or parents responsibility. The distribution and frequency of symptoms observed in our patient sample were similar to those reported in other pediatric series (27–28). Eighty percent of the discharge summaries identified a suspected trigger so these patients could receive avoidance measures. Although 90% of our patients had a single episode of anaphylaxis during the 4 years reviewed, some had 3–4 anaphylactic episodes, even patients with previously known allergies. These data stress the importance of follow-up and preventive measures.

Regarding patient identification, we could not make an accurate analysis about the improvement in the diagnoses because we did not define a specific end point in terms of diagnosis and the physicians followed the hospital's diagnostic coding system, based on the ICD-9.

The use of epinephrine increased significantly in the PEU, rising from 27 to 57.6%. However, epinephrine administration alone does not guarantee a correct diagnosis. Unlike other authors who have studied anaphylaxis treatment in the emergency department (11, 12), we have described the distinct combinations of drugs used as we believe that this more faithfully reflects the treatment received than descriptions based on separate drugs. Many patients can benefit from drugs such as antihistamines and corticosteroids, in addition to epinephrine. On reviewing the other drugs used, two notable findings stood out as follows: the reduction in the number of patients discharged without having received drug treatment and the decrease in the number of patients treated exclusively with corticosteroids. These changes are medical decisions consistent with the recognition or at least a suspicion of an anaphylactic reaction, and certain knowledge about the prognosis and proper treatment. The rate of PEOA admissions and, more important, the length of stay in the PEOA also increased significantly, rising from a median of 2 h, insufficient to guarantee a safe discharge, to a median of 9 h. This length of stay did not reach the 12 h recommended in the protocol, but is coherent with the risk of biphasic reactions described in the literature (29) and is also consistent with an increased awareness about anaphylaxis features.

On analyzing these improvements in medical performances, we also considered other factors apart from our intervention. In our patient description, we included both the distribution of clinical manifestations and the number of symptomatic patients in both groups on arrival at the PEU, in case there were any differences in the frequency or distribution of symptoms that could have influenced the physicians treating the two groups. We found no significant differences in the percentage of symptomatic patients. Moreover, the frequency and distribution of symptoms were similar in the two groups. Therefore, we believe that the differences observed can reasonably be attributed to our intervention.

Analysis of prescription of SIE revealed also significant increases after the protocol. Half of our patients were <3–

4 years old, so SIE prescription probably will not reflect accurately the number of anaphylaxis. Unfortunately, our protocol had no impact in parents' behavior. Data were available on five patients with more than one anaphylactic episode; all had epinephrine within reach but none of them used it. When asked, parents relied on previous PEU experiences that did not include epinephrine. This finding allowed us to identify a point that should be stressed in any other educational activities, including medical and/or non-health-related personnel.

Analysis of referrals to allergy specialists revealed that different decisions were taken. Overall, the percentage of patients without follow-up decreased from 69% to 22%. The number of patients referred to the allergy department increased, both from the PEU and from primary care. A correct patient identification in the PEU may have had an impact outside the hospital care.

Epinephrine adverse effects are usually a major concern among doctors treating anaphylaxis. We included side effects assessment as a clinical outcome of our study. The safety profile of the use of epinephrine in our series was good: There was one episode of palpitations after an intramuscular epinephrine dose in one patient but no specific treatment was required. Nevertheless, our study population, including otherwise healthy children without cardiovascular disease or other risk factors, does not allow us to make assumptions regarding the medical decisions with other patient profiles, such as adults with chronic or cardiovascular diseases.

A specific management protocol jointly designed by the allergy and pediatrics departments and based on the EAACI anaphylaxis guideline succeeded in improving the recognition and management of anaphylaxis in our PEU. Our study has limitations related to its observational design and the definition of cases of anaphylaxis. Despite our results, additional measures should be also considered to maintain the awareness of the PEU staff involving key elements as new junior doctors, PEU senior doctors, and triage staff, for example. Moreover, the use of epinephrine was shown to be safe in our sample of patients with anaphylaxis. Data from allergy study and more prolonged follow-up would probably provide additional information about incidence and epidemiological characteristics.

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