ORIGINAL ARTICLE

Incidence of Anaphylaxis and Subtypes of Anaphylaxis in a General Hospital Emergency Department

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Abstract

Background: The absence of large-scale international studies means that data on anaphylaxis in emergency departments in different geographic areas are still necessary.
Objective: To determine the incidence of anaphylaxis and subtypes of anaphylaxis and their distribution by age group in the emergency department of Hospital Universitario Fundación Alcorcon, Alcorcon (Madrid), Spain.
Methods: Our study was performed between 2004 and 2005. We used the definition of anaphylaxis established by the NIAID-FAAN Symposium. Patient information was collected from the electronic clinical records of the emergency department using alphanumeric strings to identify acute allergic illnesses. This strategy recovered 91.7% of all anaphylaxis episodes in a pilot study.
Results: We observed a crude cumulative incidence of 0.9 episodes of anaphylaxis per 1000 emergency episodes (95% confidence interval [CI], 0.8-1.1), and 0.8 episodes per 1000 people (95% CI, 0.7-0.9). Standardized cumulative incidence of anaphylaxis according to the Standardized European Population was 1.1 (95% CI, 0.9-1.2). On analyzing the 213 cases of anaphylaxis, we discovered that the main cause was food (28.6%), followed by drugs (28.2%), unknown causes (27.2%), *Anisakis* (10.8%), *Hymenoptera venom* (3.3%), exercise (2.4%), and latex (0.9%). Food-induced anaphylaxis was less frequent in all groups older than the 0-4 age group in both reference populations (people who attend the emergency department and the general population).
Conclusions: The cumulative incidence of anaphylaxis in our emergency department is low. Anaphylaxis by foods is more frequent in the 0-4 year group than in the other age groups. Drugs and food are the most frequent causes of anaphylaxis in our emergency department.

Key words: Incidence. Anaphylaxis. Emergency department. Subtypes.

Resumen

Fundamento: La ausencia de grandes estudios internacionales todavía hace necesario estudios de anafilaxia en los Servicios de Urgencias de diferentes áreas geográficas.
Objetivo: Determinar la incidencia de la anafilaxia y subtipos de la anafilaxia y su distribución por grupo de edades en el servicio de urgencias del Hospital Universitario Fundación Alcorcón, Alcorcón (Madrid), España.
Métodos: El estudio se realizó entre 2004 y 2005. Se utilizó la definición de anafilaxia del Simposio NIAID-FAAN. Los casos de anafilaxia se obtuvieron de la historia clínica informatizada del Servicio de Urgencia, mediante cadenas alfanuméricas que se usan para nominar enfermedades alérgicas agudas. Esta estrategia reveló 91,7% de todos los episodios de anafilaxia en un estudio piloto.
Resultados: Se observó una incidencia acumulada cruda de 0,9 episodios de anafilaxia (IC 95% 0,8-1,1) por cada 1000 episodios de emergencia, y de 0,8 (IC 95% 0,7-0,9) episodios por cada 1000 habitantes. La incidencia acumulada estandarizada según la población europea fue de 1,1 (IC 95% 0,9-1,2). Entre los 213 casos de anafilaxia, descubrimos que la causa principal fueron los alimentos (28,6%), después los medicamentos (28,2%), la anafilaxia de origen desconocido (27,2%), anisakis (10,8%), el veneno de himenópteros (3,3%), ejercicio (2,4%) y el látex (0,9%). La presencia de anafilaxia por alimentos fue menor en todos los grupos de edades mayores al grupo de 0-4 años en las dos poblaciones estudiadas (personas que asisten al servicio de urgencias y la población general).
Conclusiones: La incidencia acumulada de anafilaxia en nuestro servicio de urgencias es baja. La anafilaxia por alimentos es más frecuente en el grupo de 0-4 años que en los restantes grupos de edad. Medicamentos y alimentos son las causas más frecuentes de anafilaxia en nuestro servicio de urgencias.

Palabras clave: Incidencia. Anafilaxia. Urgencias. Subtipos.

Introduction

Anaphylaxis series have been reported at different health care levels [1-9], including emergency departments [2, 10-22], where anaphylactic reactions are generally treated [12]. However, reports on anaphylaxis in these departments are difficult to compare due to important differences in incidence, severity, cause, and management [3,10-22]. International collaboration based on uniform definitions and information on the number of emergencies attended, type of health system, distribution of emergency services at different care levels, and local health care resources makes it easier to compare studies. Financial and logistic limitations, however, mean that data from collaborations of this type will take many years to become available. Nevertheless, even if such studies could be conducted today, variations in eating habits, exposure to allergens, and drug consumption and prescribing habits would also generate disparate results.

More case series of anaphylaxis should be reported from emergency units in different geographic areas based on the variables mentioned above and on internationally accepted definitions. Our study presents the incidence of anaphylaxis in a Spanish hospital serving a predominantly urban community. Our results can add to the pool of knowledge of anaphylaxis in the emergency department in different parts of the world.

Methods

Setting

Hospital Universitario Fundación Alcorcón (HUFA) in Alcorcón (Madrid) Spain is a national health hospital with 450 beds. It is the reference emergency care center for 250 000 people in the southwest metropolitan area of the autonomous community of Madrid. In Spain, although most people have access to a national health hospital, less severe emergencies are treated at the emergency departments of primary care centers and by ambulances equipped with medical equipment and trained staff (nurse and physician). In our area, there is also a private hospital for patients with private health insurance.

Selection of Patients

A total of 217 292 people (118 571 women) were seen at our emergency department during the study period (2004-2005). Ages at the 25th, 50th, and 75th percentiles were 24, 31, and 66 years, respectively. Cases of anaphylaxis were extracted from electronic clinical records in the emergency unit using alphanumeric strings that included characters of words in Spanish to denominate acute allergic syndromes (*alerg* [allergy], *anafila* [anaphylaxis], *urtica* [urticaria], *hipersensibili* [hypersensitivity], *eritema* [erythema], *picadu* [bite], *advers* [adverse], *edem* [edema], *medica* [drug], *reacc* [reaction], *alimen* [food], *abeja* [honey bee], *avispa* [wasp]). This strategy was tested in a pilot study in which all emergency episodes from March and April 2004 were reviewed by one of the researchers. Only 1 case out of 12 was not detected using alphanumeric strings, meaning that 91.7% (95% confidence interval [CI], 61.6%-99.8%) of all anaphylaxis episodes during this period were identified.

The study was descriptive, analytic, observational, and retrospective, and was approved by the Ethics Committee for Medical Research at our institution. Informed consent was not obtained from the patients as the study was observational and consent was not required by the ethics committee.

Definitions of Anaphylaxis

We used the definition of anaphylaxis established by the NIAID-FAAN Symposium, which states that anaphylaxis is probable when any of the following criteria are satisfied: *a)* the presence of skin signs or symptoms together with respiratory involvement or signs of organic dysfunction or hypotension, *b)* the involvement of at least 2 organs or systems after recent exposure to an allergen, or *c)* signs of organ dysfunction or hypotension after exposure to a known allergen [22,23]. Although participants in this symposium believed that these criteria accurately identify anaphylactic reactions in more than 95% of cases, it was agreed that the criteria needed to be examined in a prospective multicenter clinical survey to establish their utility and determine whether further refinement was necessary.

In our analysis of clinical records, the above signs and symptoms were documented as being present and assumed to be absent if they were not reported or reported as not present. After applying the alphanumeric sequences to the electronic records for 2004 and 2005, we detected 106 520 notes with information about cases of possible anaphylaxis. We followed the Brown criteria [16] to classify anaphylaxis as severe or not severe.

As it was not possible to carry out an allergy workup of all cases in the outpatient clinic, individual etiologic agents were evaluated using emergency records and the experience and criteria of 2 experienced allergists, who agreed on the final diagnosis.

Statistics

We report the cumulative crude and standardized incidence of anaphylaxis and its causes. Incidence was calculated in relation to the number of emergencies attended in the emergency department and to the catchment population of HUFA in 2005, which was obtained from the Spanish National Institute of Statistics (www.ine.es). Direct standardized incidence was based on the European Standard Population to enable us to compare our results with those of other international studies based on populations different to ours. The odds ratios of anaphylaxis and subtypes in the different age groups were obtained by binomial logistic regression. The reference group for these regressions was the 0-4 year age group in all cases except for Hymenoptera anaphylaxis and *Anisakis* anaphylaxis, for which the reference age group was 20-29 years (first age group with cases of anaphylaxis due to these causes). We performed all analyses using Stata statistical software, version 10.0 (Stata Corp, College Station, Texas, USA).

Results

General Incidence and Incidence According to Age and Cause

The crude cumulative incidence of anaphylaxis was 0.9 episodes per 1000 emergency episodes and 0.8 episodes per 1000 people. There were 213 episodes overall. The total standardized incidence was very similar (Table 1). There were no significant differences in cumulative incidence between sexes (odds ratio [OR], 1.2 for women seen at the emergency department; 95% CI, 0.8-1.5; OR, 1.03 for women in the general population; 95% CI, 0.8-1.4).

The distribution of the cumulative incidence of anaphylaxis differed with age, depending on whether the number of emergencies or the general population was used as a reference. When the number of emergencies was used, logistic regression showed that the patients aged 5 to 9 years (OR, 0.3), 20 to 29 years (OR, 0.4), 30 to 39 years (OR, 0.5), and >69 years (OR, 0.3) had a lower risk of attending the emergency department due to anaphylaxis than the reference age group (0-4 years) (Table 2). However, when the general population of our health care district was used as the reference group, there was a peak in incidence in the 0-4 year age group (2.2 per 1000 people). The cumulative incidence of the other age groups was under 1 per 1000 people in all cases.

On analyzing the 213 cases of anaphylaxis, we discovered that the main cause was food (28.6%), followed by drugs (28.2%), causes of unknown origin (27.2%), *Anisakis* (10.8%), *Hymenoptera* venom (3.3%), exercise (2.4%), and latex (0.9%). Logistic regression models showed that the causes of anaphylaxis were distributed differently by age group, especially when the total number of emergencies was used as the reference. In this case, food-induced anaphylaxis was less frequent in patients aged over 20 years (OR, 0.04-0.3), unknown causes were more frequent in the 15-19 year group (OR, 4.4; 95% CI, 1.1-17.7) and the 40-49 year group (OR, 4.1; 95% CI, 1.2-14.5), and *Anisakis* anaphylaxis was more frequent in the 40-49 year group (OR 9.7; 95% CI, 1.1-83.0) and the 50-59 year group (OR, 15.9; 95% CI, 1.9-127.1). Only anaphylaxis of unknown origin was less frequent among men (OR adjusted for age, 0.5; 95% CI, 0.3-0.9) (Table 2).

However, when the reference population was the general population, we noticed differences only in food anaphylaxis, for which all age groups had a lower incidence than the 0-4 year group.

Drugs and Food as Causes of Anaphylaxis by Age Group

In children aged 0 to 4 years, the main foods responsible for anaphylaxis were, in order, cow's milk, hen egg, fruit, and fish (responsible for 81.4% of all episodes of food-induced anaphylaxis). In patients aged 5 to 29 years, complex foods, fish, fruit, and shellfish were responsible for 66.6% of all episodes (Table 3). The principal causes of anaphylaxis in patients aged 30 to 69 years were fish, fruit, and tree nuts (78.9% of all episodes in this age range). The term complex foods refers to foods manufactured with many different and sometimes unknown components or a meal cooked with several ingredients where it is not possible to discover the culprit allergen.

In patients aged 5 to 29 years, drug-induced anaphylaxis was mainly due to nonsteroidal anti-inflammatory drugs (NSAIDs); the principal causes in this category were acetylsalicylic acid and metamizole (44.4% of all cases of anaphylaxis by drugs) (Table 4). In the 30-69 year group, metamizole, ibuprofen, acetylsalicylic acid, and aceclofenac accounted for 47.8% of all cases. In this group, antibiotics, especially amoxicillin-clavulanic acid and amoxicillin, were also frequent causes of anaphylaxis (25% of all cases), and in patients older than 69 years, NSAIDs were again the main cause (62.5% of all cases) (Table 4).

Oral administration was the most common route of administration among patients with drug-induced anaphylaxis (88.3%), and 87.9% of episodes were caused by the first dose.

Severity of Anaphylaxis

Mucocutaneous and lower respiratory signs or symptoms were the most frequent clinical findings, whereas nasal and neurological findings were the least frequent (Table 5); 26.3% of anaphylactic episodes were classified as severe.

Discussion

In our study, the cumulative incidence of anaphylaxis was low (0.9 episodes per 1000 emergency episodes and 0.8 episodes per 1000 people) compared with other series of emergency department anaphylaxis (range, 0.35-3.33 episodes per 1000 emergencies) based on a similar definition to

Table 1. Cumulative Incidence of Anaphylaxis in the Emergency Department of Hospital Universitario Fundacion Alcorcon Between 2004 and 2005

Age Group, y	General Cumulative Incidence per 1000 Episodes	95% CI (Lower)	95% CI (Upper)	General Cumulative Incidence per 1000 People	95% CI (Lower)	95% CI (Upper)
0-4	1.6	1.1	2.2	2.2	1.4	2.9
4-9	0.5	-0.1	1.0	0.2	-0.03	0.5
15-14	1.3	0.3	2.2	0.6	0.2	1.1
15-19	0.9	0.3	1.6	0.6	0.2	1.1
20-29	0.7	0.4	0.9	0.6	0.4	0.8
30-39	0.8	0.6	1.1	0.6	0.4	0.9
40-49	1.7	1.1	2.3	0.9	0.6	1.3
50-59	1.4	0.9	1.9	0.8	0.5	1.1
60-69	1.0	0.6	1.5	0.8	0.5	1.2
>69	0.6	0.3	0.8	0.9	0.5	1.4
Total crude incidence	0.9	0.8.	1.1	0.8	0.7	0.9
Total standardized incidence	1.1	0.9	1.2			

Abbreviation: CI, confidence interval.

ours [3,10-22, 24]. We discovered several peaks in incidence in different age groups (0-4 and 40-49 years), especially when the denominator of incidence was the number of emergencies. We also found that the 3 main causes of anaphylaxis were food (28.6%), drugs (28.2%), and unidentified causes (27.2%); only 26.3% of patients experienced severe anaphylaxis.

Reasons other than differences in the definition of anaphylaxis should thus be sought to explain the considerable differences in incidence between our study and others. Possible reasons are differences in age ranges (children or adults), methods used to select possible cases (coded diagnosis [IC-9-M], search for alphanumeric sequences, exhaustive review of all clinical records from a specific period), emergency department attendance habits in different health care systems, or the number of health care access points. In addition, to our knowledge, none of the studies published have reported the accuracy of the strategies used [3,10-22,25], thus making it impossible to know whether the reported data are a reliable estimation of the incidence of anaphylaxis in emergency departments. In our case, the strategy of using alphanumeric strings retrieved almost 92% of anaphylaxis cases in the 2 months when our strategy was tested.

A low ratio of anaphylaxis episodes to the total number of emergencies seen in our emergency department can explain the lower incidence detected in our study. This ratio may have been reduced by several factors including consumption habits specific to our population, the large number of emergency department visits in our hospital, and the fact that access to health care resources other than our emergency department may be limited. Although the ratio detected in our series was lower than that of other published series, the correlation between the number of emergencies attended and cumulative incidence reported by these series is not significant [3, 10-22] (data not shown).

We observed differences in the distribution of the cumulative incidence of anaphylaxis according to age, and these differences were particularly pronounced when the denominator of incidence was the number of emergencies. The peaks in such cases were between 1.6 and 1.7 per 1000 emergencies (0-4 and 40-49 age groups). Gaeta et al [12] used a national survey to estimate the incidence of acute allergic reactions (including anaphylaxis) in general and short-stay hospitals throughout the United States, and reported the highest incidence (>10.5 cases per 1000 emergencies) in patients aged 20 to 70 years. One possible explanation for the differences between our findings and those of Gaeta et al is the fact that in their case, patient selection was based on IC-9-M codes for acute allergic syndromes, with no further refinement of data, whereas in our case, only patients with anaphylaxis were selected. However, when the general population was used as a reference, we detected a peak only in the 0-4 age group (2.2 cases per 1000 people) (the incidence in the other age groups was <1 case per 1000 people in all cases). In the study by Gaeta et al, the rate per 1000 population was also higher than in our study (overall 3.8), with no peak in the 0-4 year group. In our study, the lack of peaks in incidence in the general population older than 4 years and the presence of these peaks in the emergency department population may be related to a lower percentage of emergency department visits by

Table 2. General Cumulative Incidence of Anaphylaxis and Subtypes[a]

Age Group, y	Percentage of Emergencies Compared With General Population	General Cumulative Incidence per 1000 Emergencies	General Cumulative Incidence per 1000 People	Drugs per 1000 Emergencies	Drugs per 1000 People	Unknown Causes per 1000 Emergencies	Unknown Causes per 1000 People	*Hymenoptera* per 1000 Emergencies	*Hymenoptera* per 1000 People	Foods per 1000 Emergencies	Foods per 1000 People	*Anisakis* per 1000 Emergencies	*Anisakis* per 1000 People
0-4	133.5%	1.6	2.2[a]	0.2	0.3	0.2	0.2			1.3	1.8		
4- 9	51.8%	0.5[a]	0.2							0.5	0.2[a]		
10-14	4.7%	1.3	0.6			0.6	0.3			0.6	0.3[a]		
15-19	68.1%	0.9	0.6	0.1	0.1	0.7[a]	0.5						
20-29	89.7%	0.7[a]	0.6	0.2	0.2	0.3	0.3	0.03	0.02	0.2	0.2[a]	0.03	0.02
30-39	77.9%	0.8[a]	0.6	0.3	0.2	0.3	0.3	0.03	0.02	0.2	0.1[a]	0.1	0.1
40-49	56.5%	1.7	1.0	0.5	0.3	0.7[a]	0.4			0.3	0.2[a]	0.3[a]	0.1
50-59	59.9%	1.4	0.8	0.5	0.3	0.2	0.1			0.4	0.2[a]	0.4[a]	0.2
60-69	78.7%	1.0	0.8	0.3	0.3	0.4	0.3	0.1	0.1	0.1	0.04[a]	0.2	0.1
>69	169.8%	0.6[a]	1.0	0.2	0.4	0.1	0.2	0.1	0.1	0.1	0.1[a]	0.03	0.05
Males	75.5%	0.9	0.8	0.3	0.2	0.2	0.2	0.2	0.05	0.1	0.3	0.4[a]	0.1
Females	90.2%	1.1	0.8	0.3	0.2	0.4	0.2	0.4	0.03	0.1	0.2	0.2	0.1

[a]Significant differences between age groups with logistic regression models.

Table 3. Foods Involved in Anaphylaxis by Age Group[a]

0-4 y	No. of Patients	%	5-29 y	No. of Patients	%	30-69 y	No. of Patients	%
Cow's milk	12	44.4	Complex food	3	20.0	Fish	10	52.6
Hen egg	6	22.2	Fish	3	20.0	Fruits	3	15.8
Fruits	2	7.4	Cow's milk	2	13.3	Nuts (hazelnuts and walnuts)	2	10.5
Fish	2	7.4	Shellfish	2	13.3	Milk	1	5.3
Nuts (almond)	1	3.7	Hen egg	1	6.7	Hen egg	1	5.3
Cereals without gluten	1	3.7	Legumes	1	6.7	Shellfish	1	5.3
Sunflower seeds	1	3.7	Pitaya fruit	1	6.7	Complex foods (including almond)	1	5.3
Vanilla	1	5.4	Chicken	1	6.7			
Unknown foods	1	3.7	Fruits	1	6.7			
Total	27	100.0	Total	15	100.0	Total	19	100.0

[a]Food anaphylaxis was not detected in patients aged over 69 years.

Table 4. Most Common Drugs Involved in Anaphylaxis by Age Group

0-4 y	No.[a]	%	5-29 y	No.[a]	%	30-69 y	No.[a]	%	>69 y	No.[a]	%
Cyanocobalamin	2	50.0	Acetylsalicylic acid	2	22.2	Metamizole	8	22.2	Metamizole	2	25.0
Cefaclor	1	25.0	Metamizole	2	22.2	Amoxicillin-Clavulanic Acid	6	16.7			
Albuterol	1	25.0	Immunotherapy with allergen extracts	1	11.1	Ibuprofen	4	11.1	Diclofenac	2	25.0
			Clindamycin	1	11.1	Acetylsalicylic acid	3	8.3	Ibuprofen	1	12.5
			Pyrazinamide	1	11.1	Amoxicillin	3	8.3	Cloxacillin	1	12.5
			Ibuprofen	1	11.1	Aceclofenac	2	5.6	Ciprofloxacin	1	12.5
			Ketorolac	1	11.1	Codeine + acetaminophen + ascorbic acid	1	2.8	Doxazosin	1	12.5
						Diclofenac Misoprostol	1	2.8			
						Celecoxib	1	2.8			
						Iodinated contrast media	1	2.8			
						Dextromethorphan	1	2.8			
						Diclofenac	1	2.8			
						Piroxicam	1	2.8			
						Misoprostol-ibuprofen	1	2.8			
						Levofloxacin	1	2.8			
						Doxazosin	1	2.8			
Total	4	100.0	Total	9	100	Total	36	100.0	Total	8	100.0

[a]No. of patients.

patients aged over 4 years. Such an effect would decrease the denominators of the emergency population and, consequently, increase the cumulative incidence of anaphylaxis in emergency visits (Table 2).

We found that the distribution of incidence peaks according to age group was different in both reference populations (emergency and general) for anaphylaxis caused by food but not by other factors. Nevertheless, the distribution of subtypes of anaphylaxis differed according to age group: food was responsible for peaks in the 0-4 year group (78% of cases), while drugs and unidentified causes (68% of cases) were responsible in the 40-49 year group; finally, food, *Anisakis*, drugs, and unknown causes (100% of cases) were responsible for peaks in the 50-59 year group. These distributions of incidence are related to the epidemiology of these triggers. Food allergies (mainly to cow's milk and hen egg) are most common in the early years of life [26], while drug allergy is more common among adults [27]. On the other hand, patients with anaphylaxis due to unknown causes tend to be young or middle-aged [28] and female (65%-72%) [29]. In the case of *Anisakis*, sensitization has been found to increase with age throughout Spain [30].

We found that the 3 main causes of anaphylaxis were food (28.6%), drugs (28.2%), and unknown causes (27.2%). In most series of anaphylaxis, drugs and food are the main causes of episodes seen in the emergency department. One of the main differences in other series is the higher percentage of *Hymenoptera* venom anaphylaxis, which ranges from 7.1% to 29.0% [3,10,13,16] depending on the prevalence of *Hymenoptera* allergy in the catchment areas analyzed. Our hospital is located in an urban area with few beekeepers, hence the low incidence of *Hymenoptera* anaphylaxis in our series. Another difference between our series and other series published to date is the high incidence of Anisakis anaphylaxis, a subtype that has not been reported in series outside Spain [2, 10-22]. Anaphylaxis due to *Anisakis* has been reported by Spanish researchers [31], especially in regions of Spain where ingestion of uncooked fish is more frequent [30].

NSAIDs and antibiotics are the 2 main causes of drug-induced anaphylaxis and ß-lactams the most common cause (25%-75%) within the group of antibiotics. Only Pastorello et al [11] have reported on NSAIDs and anaphylaxis, and their results differ considerably from ours, mainly due to differences in consumption habits, which vary between countries. These differences are probably larger for NSAIDs than for antibiotics. In our series, only 26.3% of patients had severe anaphylaxis, contrasting sharply with the proportion of almost 70%—the highest to be published to date—reported by Pastorello et al.

Like previously published studies in this area, our study is limited by its retrospective design, which prevented exhaustive data collection.

In summary, using alphanumeric strings to select patients with anaphylaxis has proven to be a very accurate method of case selection. Furthermore, the cumulative incidence of anaphylaxis detected in our emergency department is low compared to other series that have used similar definitions. Our analysis of incidence in the general population and the emergency department population revealed a peak in incidence only in the 0-4 year group in both cases. The distribution of the different causes of anaphylaxis in different age groups is associated with the epidemiology of allergy to the different allergens. The predominance of food, drugs, and *Anisakis* as causes of anaphylaxis and the low percentage of anaphylaxis to *Hymenoptera* venom found in our study are related to specific exposure patterns in our area.

Table 5. Systems and Organs Involved in Anaphylaxis Episodes

Clinical Features	No. of Patients	%
Mucocutaneous involvement	204	95.8
Urticaria	143	67.1
Angioedema	88	41.3
Erythema	16	7.5
General itching	71	33.3
Lingual edema	15	7.0
Uvular edema	21	9.9
Cardiovascular involvement	88	41.3
Low oxygen saturation <92	43	20.2
Bradycardia	3	1.4
Cyanosis	5	2.4
Syncope	7	3.3
Ischemic electrocardiographic signs	1	0.5
Arrhythmias	2	0.9
Dizziness	35	16.4
Malaise	14	6.6
Blood pressure <100	28	13.2
Digestive involvement	93	43.7
Abdominal pain	47	22.1
Vomiting	44	20.7
Diarrhea	18	8.5
Nausea	6	2.8
Dysphagia	20	9.4
Neurovascular involvement	10	4.7
Loss of consciousness	1	0.5
Paresthesias	2	0.9
Seizures	1	0.5
Incontinence	2	0.9
Decreased consciousness	2	0.9
Weakness	1	0.5
Upper respiratory tract involvement	61	28.6
Hoarseness	21	9.9
Stridor	14	6.6
Difficulty swallowing	31	9.4
Laryngeal edema	4	1.9
Lower respiratory tract involvement	133	62.4
Cough	20	9.4
Dyspnea	125	58.7
Wheezing	23	10.8
Thoracic pain	7	3.3

Acknowledgements

This study was supported by grant number PI 051744 from the Fondo de Investigación Sanitaria (Spanish Ministry of Research and Technology) and a grant from the Fundación Mutua Madrileña (official announcement 2005).

Previous Presentation: Data from this manuscript have been presented at the XXVI Congress of the European Academy of Allergology and Clinical Immunology. Goteborg, Sweden from June 9-13, 2007; the 65th Anniversary Meeting of American Academy of Allergy Asthma and Immunology in Philadelphia, USA from March 14-19, 2008; and the XXVI National Congress of the Spanish Society of Allergy and Clinical Immunology in Bilbao, Spain from November 6-8, 2008.

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Manuscript received February 10, 2010; accepted for publication, May 17, 2010.

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