

Characteristics of anaphylaxis in children referred to a tertiary care center

Emine Vezir, M.D., Mustafa Erkoçoğlu, M.D., Ayşenur Kaya, M.D., Müge Toyran, M.D., Celal Özcan, M.D., Ayşegül Akan, M.D., Dilek Azkur, M.D., Tayfur Giniş, M.D., Ersoy Civelek, M.D., and Can Naci Kocabaş, M.D.

ABSTRACT

Anaphylaxis is a potentially life-threatening condition. There are limited data about the etiology and the clinical characteristics in developing countries. This study aimed to investigate the clinical characteristics of anaphylaxis patients attending our pediatric allergy clinic. We conducted a prospective analysis of patients who were admitted to our allergy clinic for anaphylaxis from 2010 to 2012. Ninety-six patients were evaluated during the study period. The mean age was 7.4 ± 5.2 years. Venom, food, and drugs were the most common causative agents responsible for 31 (32.3%), 30 (31.3%), and 26 (27.1%) of the cases, respectively. Foods implicated most frequently were peanuts and nuts ($n = 9$; 30.0%), cow's milk ($n = 7$; 23.3%), and egg white ($n = 6$; 20.0%). The clinical manifestations during anaphylaxis in order of frequency were cutaneous (97.9%), respiratory (86.5%), gastrointestinal (42.7%), neurological (37.5%), and cardiovascular symptoms (30.2%). A biphasic course was noticed in five cases (5.2%). Of the 91 patients, 79 (86.8%) received H_1 -antihistamines, 73 (80.2%) received corticosteroids, 40 (44.4%) received adrenaline, 38 (41.8%) received fluid replacement therapy, 18 (19.8%) received β_2 -mimetics, and 8 (8.8%) received H_2 -antihistamines. According to severity, 7.3% of patients had mild, 59.4% had moderate, and 33.3% had severe anaphylaxis. Food and bee venom allergy were the most common etiologies. Adrenaline, the first-line treatment of anaphylaxis, was administered in only 44.4% of our cases.

(Allergy Asthma Proc 34:239–246, 2013; doi: 10.2500/aap.2013.34.3654)

Anaphylaxis is a serious, life-threatening systemic hypersensitivity reaction that might cause death and the diagnosis is based on clinical history and physical findings.^{1,2} Most studies that focused on the epidemiological characteristics, clinical features, and management of anaphylaxis were conducted on adults or general populations.^{3–14} However, anaphylaxis is more common during childhood and a large number of new cases occur among children and adolescents every year.^{15,16} There are a wide variety of triggers for anaphylaxis and their frequency varies according to age.⁴ Generally, foods are the most common cause of anaphylaxis in childhood, whereas medication and insect sting anaphylaxis are more common in adults.¹⁷ Many of the triggers for anaphylaxis are universal; however, some important geographic variations have also been reported. Food triggers differ according to local dietary habits, specific food exposures, and methods of food preparation.¹⁸ Insect populations differ between geo-

graphic regions. Therefore, the frequency of venom anaphylaxis can vary.¹⁹

There are limited data about anaphylaxis in children. To make a better description of the characteristics of anaphylaxis and to improve management, we prospectively evaluated children admitted to our clinic with a suspicion or diagnosis of anaphylaxis.

MATERIALS AND METHODS

Definition of Anaphylaxis and Severity Grading

The diagnosis of anaphylaxis was defined and classified according to the criteria suggested in the European Academy of Allergy and Clinical Immunology Taskforce on the management of anaphylaxis in childhood.²⁰

Collection of Data

From January 1, 2010 until July 30, 2012, we prospectively collected data on all consecutive patients who were admitted for investigation of anaphylaxis to our outpatient clinic. All patients were evaluated by a pediatric allergist. A detailed history was taken using standardized questions including (1) demographic data; (2) detailed information on the symptoms of anaphylaxis, with separate questions for dermatologic, respiratory, gastrointestinal, cardiovascular, and behavioral or neurological symptoms; (3) the trigger of anaphylaxis, investigations used to confirm the implication of

From the Department of Pediatric Allergy and Clinic Immunology, Ankara Children's Hematology Oncology Education and Research Hospital, Ankara, Turkey
The authors have no conflicts of interest to declare pertaining to this article
Address correspondence and reprint requests to Can Naci Kocabaş, M.D., Department of Pediatric Allergy and Clinic Immunology, Ankara Children's Hematology Oncology, Education and Research Hospital, Altındağ, Ankara 06100, Turkey
E-mail address: cankocabas@yahoo.com
Copyright © 2013, OceanSide Publications, Inc., U.S.A.

the trigger; (4) the course of anaphylaxis, time lapse between contact with the trigger and onset of subsequent symptoms, total duration of symptoms, biphasic course, or not; (5) the treatment of anaphylaxis and time lapse between onset of symptoms and administration of medication; (6) exposure to the same agent before and previous reaction; and (7) coexistence of allergic disease.

Identification of the Trigger

Both skin-prick tests (SPTs) and/or specific IgE for the suspected etiologic agent were performed for patients whose parents gave permission. When at least one of these tests was positive and the history was compatible, the agent was defined as the allergic agent. When both were negative, intradermal tests were performed where available. Oral provocation tests were undertaken for patients whose story was doubtful for the relation of the allergen with anaphylaxis. When we could not reveal a proven etiology, patients were labeled as "idiopathic anaphylaxis."

SPT, specific IgE, Provocation

Depending on each individual case SPTs were performed with one or more of the following: (1) a commercial extract of suspected food and also with standard inhalant allergens (common grass, weed, tree, and cereal pollens, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Alternaria*, and cat and dog dander; Stallergenes SA, Antony, France), (2) yellow jacket wasp or honey bee venom extract (Soluprick; ALK, Madrid, Spain) in a concentration up to 300 µg/mL, (3) self-prepared serial dilutions of amoxicillin and dap penicillin kit (Diater, Madrid, Spain), and (4) fresh sample of suspected food by means of prick-to-prick testing. SPTs were performed on the back or on the volar side of the forearm by means of a micro lance (staller point) and read after 15 minutes. Histamine HCL (Stallergenes SA) and teomin negative (Stallergenes SA) were used as positive and negative controls, respectively. Results were assessed as positive if the wheal mean diameter was 3 mm or more than the reaction of the negative control. Allergen-specific IgE levels were measured using the CAP-system (Phadia, Uppsala, Sweden).

In case a proven etiology could not be determined by history and SPT and/or sIgE, open provocation testing was performed with the suspected agent (drug or food).

All medical procedures (*i.e.*, allergen-specific immunotherapy, contrast medium, and blood products) are labeled as drugs. Anaphylaxis occurring at school, restaurants, and outdoors are labeled as "outside."

The Ethical Committee of our hospital approved the study; all participants (or their parents) provided written informed consent.

Table 1 Patient characteristics

Characteristics	No. of Children (%)
Gender	
Male	61 (63.5)
Female	35 (36.5)
Age ranges (yr)	
0–2	20 (21.5)
3–6	25 (26.9)
7–11	21 (22.6)
≥12	27 (29.0)
Concurrent allergic disease	45 (48.4)
Asthma	35 (37.6)
Allergic rhinitis	17 (18.3)
Atopic dermatitis	14 (15.1)
Familial history of atopic diseases	32 (34.4)
Severity of anaphylaxis	
Mild	7 (7.3)
Moderate	57 (59.4)
Severe	32 (33.3)
Exposure to the same agent before	58 (69.9)
Reaction during previous exposure	
No reaction	16 (28.1)
Anaphylaxis	26 (45.6)
Allergic reaction other than anaphylaxis	15 (26.3)

Statistical Analysis

All analysis performed using SPSS statistical software Version 17 (SPSS, Inc., Chicago, IL). A descriptive analysis was used for the characterization of the study population. The children were grouped according to age (0–2 years, 3–6 years, 7–11 years, and ≥12 years), gender (male/female), triggers (hymenoptera venom, foods, and drugs), atopic status (having allergic disease as atopic and having not nonatopic), and severity (mild–moderate and severe). The groups were compared with Pearson chi-square test or Fisher's exact test and Mann-Whitney *U* test where suitable. A value of $p < 0.05$ was considered statistically significant.

RESULTS

Demographic Data and Place of Occurrence

Ninety-six patients were diagnosed to have anaphylaxis. The characteristics of the participants are shown in Table 1. The mean age was 7.4 ± 5.2 years. Anaphylaxis was significantly more frequent in boys ($p < 0.001$). There was no difference in terms of gender between age groups ($p > 0.05$). Anaphylaxis occurred at home in 47.2% of the cases, outside in 31.5% patients, and in the hospital in 21.3% of the cases. In children aged 0–2 years, anaphylaxis occurred mostly at home

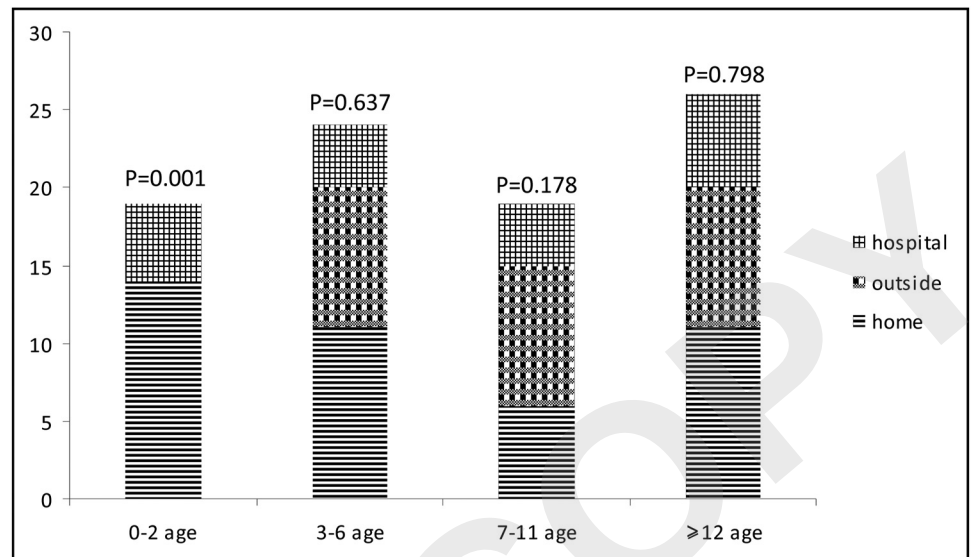


Figure 1. Age distribution and place of occurrence of anaphylaxis.

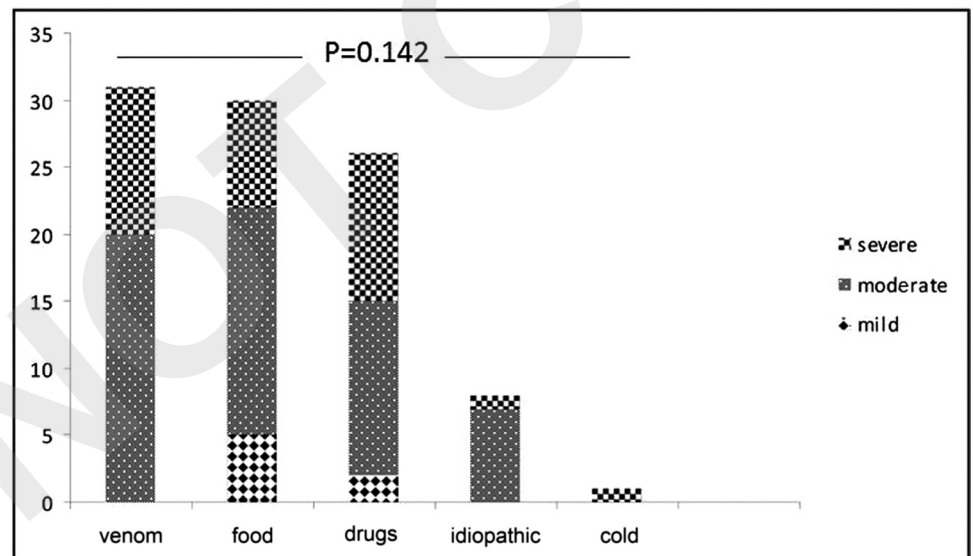


Figure 2. Severity of anaphylaxis according to trigger.

($p = 0.001$); there was no difference among other age groups (Fig. 1).

Severity Groups

Seven (7.3%) of the anaphylaxis cases were classified as mild, 57 (59.4%) as moderate, and 32 (33.3%) as severe (Table 1). These severity groups were separated as mild-moderate and severe for better statistical analysis. There was no difference between the severity groups according to gender ($p = 0.549$), age ($p = 0.190$), and the place where anaphylaxis occurred ($p = 0.564$). One near fatal reaction was reported, but there were no fatalities. Cardiovascular and neurological manifestations were more common in the severe group ($p < 0.001$ and $p = 0.002$), whereas respiratory system presentation was more common in mild-moderate group ($p = 0.020$).

There was no significant difference between the severity groups according to etiology (Fig 2). The frequency of exposure to the same agent before and history of previous anaphylaxis was also not different between severity groups ($p = 0.406$ and $p = 0.466$, respectively). The frequency of receiving epinephrine, corticosteroid, and H_2 -antihistamines at presentation was not different between the mild-moderate and severe anaphylaxis groups. The administration of fluid replacement was more frequent among children with severe anaphylaxis ($p = 0.013$) and use of H_1 -antagonist was more frequent among patients with mild-moderate disease ($p = 0.001$).

Symptoms of Anaphylaxis

The clinical manifestations during anaphylaxis in order of frequency were cutaneous (97.9%), followed by

Table 2 Diagnostic tests used to confirm the implication of trigger in 88 cases with an identified trigger

Trigger (no. of cases)	SPT <i>n</i> positive/ <i>n</i> performed	Intradermal Test <i>n</i> positive/ <i>n</i> performed	CAP	Provocation
Food (30)				
Honey (2)	1/2	—	1/1	—
Fish (3)	2/3	—	2/3	—
Legumes (3)	3/3	—	1/1	—
Nuts (8)	8/8	—	8/8	—
Cow's milk (7)	7/7	—	7/7	—
Egg-white (6)	6/6	—	6/6	—
Drugs (26)				
Antibiotics (15)	0/3	2/3	—	—
NSAID (3)	0/2	—	—	2/2
Antiepileptic (1)	—	—	—	—
Local anesthetic (1)	—	—	—	—
Others (6)	1/3	1/2	—	1/1
Hymenoptera venom (31)				
Wasp (20)	6/14	6/6	18/18	—
Honey bee (9)	3/8	1/1	7/8	—

NSAID = nonsteroidal anti-inflammatory drug; SPT = skin-prick testing; CAP = CAP system testing.



Figure 3. Trigger of anaphylaxis.

respiratory (86.5%), gastrointestinal (42.7%), neurological (37.5%), and cardiovascular symptoms (30.2%). The frequency of system involvement was not different between age groups.

Triggers of Anaphylaxis

The etiologic agent was identified by history in 21 children. A diagnostic workup for the etiology of anaphylaxis was performed in 75 children. Skin tests (epidermal and/or intradermal) yielded positive results in 48 of 69 children tested. A serum-specific IgE was found positive in 52 of 60 children. In five children, a

provocation test was performed and two of them were negative (Table 2).

The anaphylactic trigger was identified in 88 cases (91.6%), whereas it was unknown or unclear in 8 (8.3%). Venom, food, and drugs were the most common causative agents: 31 (32.3%), 30 (31.3%), and 26 (27.1%) cases, respectively (Fig. 3). Foods implicated most frequently were peanut and nuts ($n = 9$; 30.0%), cow's milk ($n = 7$; 23.3%), and egg white ($n = 6$; 20.0%). Hymenoptera venom anaphylaxis was caused by yellow jacket venom in 18 patients (66.7%) and honey bee in 9 (33.3%). The drugs implicated most frequently

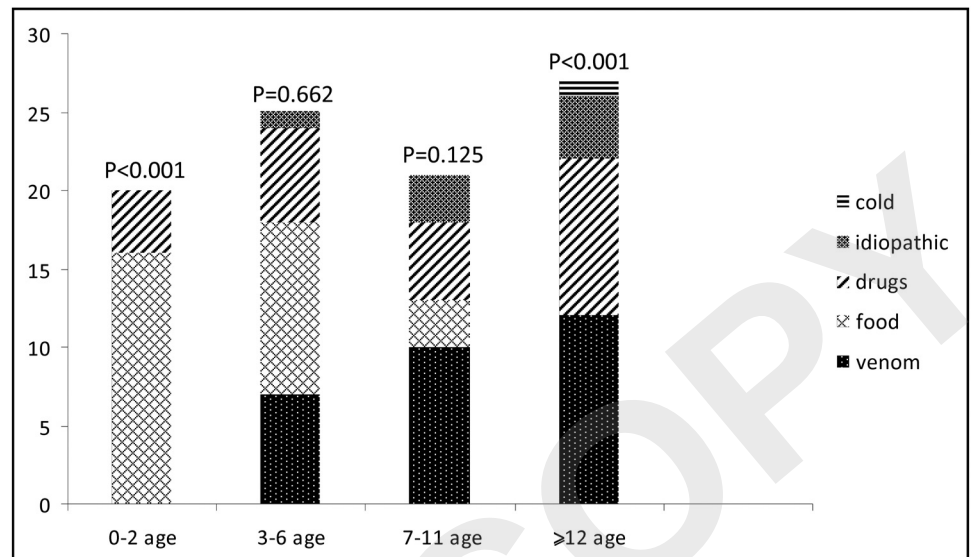


Figure 4. Trigger of anaphylaxis in different age groups.

were antibiotics ($n = 15$; 57.7%) and nonsteroidal anti-inflammatory drugs ($n = 3$; 11.5%). Exercise and latex did not contribute to the occurrence of anaphylaxis in our study group.

Route of exposure was oral in 37.5%, cutaneous in 33.3%, i.v. in 11.5%, intramuscular in 6.3%, subcutaneous in 2.1%, and respiratory in 1.0% of cases.

The frequency of etiologic agents according to age groups is given in Fig. 4. When compared according to gender there was no difference according to etiologic agents ($p = 0.347$).

Recurrence of Anaphylaxis

Fifty-eight patients (69.9%) had a previous exposure to the same agent and 40% of these patients ($n = 26$) had anaphylaxis (46.1% with food, 34.6% with hymenoptera venom, and 15.3% with drugs); 23.1% ($n = 15$) had experienced allergic reactions other than anaphylaxis (such as urticaria, angioedema, and erythema; 26.6% with food, 40.0% with hymenoptera venom, and 33.3% drugs) previously. In detail, 20 of 31 subjects with bee venom anaphylaxis had experienced a bee sting before, 9 of them had anaphylaxis, 3 of them had large local reactions, and 3 had angioedema during their previous sting. Twenty of 30 subjects with food anaphylaxis had exposure to the same food previously; 11 of them had anaphylaxis, 2 of them had urticaria, and 1 of them had angioedema. Sixteen of 26 patients with drug anaphylaxis had experienced the same drug before; 4 of them had anaphylaxis and 3 of them had angioedema. The number of anaphylactic episodes was significantly higher among patients with concurrent allergic disease when compared with patients without (2.45 ± 2.9 versus 1.3 ± 0.6 ; $p = 0.040$).

Course of Anaphylaxis

The median time lapse between contact with the trigger and onset of symptoms was 10 minutes (5–18 minutes; median, 25–75%). The total duration between onset of symptoms and complete recovery was 2 hours (1–5 hours; median, 25–75%).

A biphasic course was noticed in five cases (5.2%), with a symptom-free interval between a minimum of 30 minutes and maximum of 9 hours. One of the patients with biphasic reaction was in the 0- to 2-year age group and four were >7 years old. Three of the patients were girls. Etiologic agent was drugs in three and hymenoptera venom in two. One patient was at home, two were at the hospital, and two were outdoors when anaphylaxis occurred. All patients with biphasic anaphylaxis had only one episode of anaphylaxis until now. Mucocutaneous, respiratory, and cardiovascular system involvements were present in four of five patients. Gastrointestinal system and neurological system involvements were present in two. Four patients with biphasic reaction had severe anaphylaxis ($p = 0.035$). Concurrent allergic disease was present in only one patient with biphasic anaphylaxis. All of the patients with biphasic reaction had received fluid replacement therapy ($p = 0.009$).

Treatment of Anaphylaxis

Of the 91 patients who could give information on the treatment of anaphylaxis, 79 (86.8%) received H_1 -antihistamines, 73 (80.2%) received corticosteroids, 40 (44.4%) received epinephrine, 38 (41.8%) received fluid replacement therapy, 18 (19.8%) received β_2 -mimetics, and 8 (8.8%) received H_2 -antihistamines. Epinephrine was used by subcutaneous route in two patients, i.v. route in three patients, and intramuscularly in 34 cases.

In two patients, no medication was used. Only two patients needed intensive care.

Time lapse between onset of symptoms and first administration of medication was recorded in 79 of 96 patients, which ranged from 1 to 1440 minutes (mean, 54.9 minutes; median, 15 minutes). In 28 of 32 cases with severe anaphylaxis, this time lapse ranged from 1 to 720 minutes (mean, 48.1 minutes; median, 15 minutes). In 49 of 64 cases with mild-moderate anaphylaxis it ranged from 1 to 1440 minutes (mean, 58.7 minutes; median, 15 minutes).

Atopic Status

Forty-five children (48.4%) had a personal history of atopic disease (Table 1).

Children with food anaphylaxis had a higher rate of concurrent allergic diseases (74.1%) than patients affected by other etiologic agents (37.9%; $p = 0.02$). The rate of atopic diseases was not different between patients with anaphylaxis caused by drugs and hymenoptera venom ($p = 0.087$ and $p = 0.128$, respectively).

DISCUSSION

This study presents the etiology and the characteristics of the patients who were diagnosed with anaphylaxis in the pediatric allergy clinic of our hospital. We revealed that anaphylaxis occurred in an out of the hospital setting in the majority of cases and were mostly triggered by Hymenoptera venom and foods in children. Unfortunately, it was shown that most of the children did not receive adequate treatment.

In accordance with other investigations in children,²¹⁻²⁸ anaphylaxis was significantly more frequent in boys in our study and home was the most frequent location of occurrence of anaphylaxis.²¹⁻²³ Number of episodes occurring at home and out of home was similar for patients >2 years old, stressing the importance of having rescue medication available at any place.²⁹ Like most studies, we revealed that anaphylaxis was moderate in severity most frequently.^{6,21,22,30} In a recent study where children were evaluated retrospectively from electronic records, mild anaphylaxis was reported to be the most frequent.³¹ The difference may be caused by the use of different criteria used to define severity groups. Furthermore, milder symptoms of anaphylaxis might be underrecognized and not referred to an allergy clinic. The data about the clinical characteristics of anaphylaxis assessed according to different severity groups is limited. In accordance with our results, severity was reported to be similar between age groups in one report.³¹ We have revealed that etiology, the time lapse between occurrence of symptoms and treatment, frequency of exposure to the same agent before, and history of previous anaphylaxis were not different between severity groups.

The two most frequent symptoms involved mucocutaneous (97.9%) and respiratory (86.5%) system in our study. This is in accordance with other investigations of anaphylaxis in children.^{7,21-24} However, in some studies including both adults and children, cardiovascular symptoms were the second most prevalent instead of respiratory system.³⁴ In our study frequency of other system involvements were gastrointestinal (42.7%), neurological (37.5%), and cardiovascular (30.2%), and these frequencies vary among studies.^{3,21,22,24} Such variability in the symptoms might be caused by the differences in the methodology of the studies, definitions, and assessments of the clinical findings and study populations.

In accordance with previous studies,³² an IgE-mediated mechanism against a suspected trigger of anaphylaxis could be confirmed in more than one-half (59.3%) of the children. The most prevalent etiology of anaphylaxis was hymenoptera venom (32.3%), with the majority of cases occurring due to wasps (66.7%). The rate of Hymenoptera venom anaphylaxis was higher than the rates reported in previous studies.^{4,5,7,22,24,31,33} The reason for the high rate might be that bee venom allergy is well known and can be recognized more easily. Furthermore, beekeeping is widespread and wasps are common in the environment in our country.

The second leading cause of anaphylaxis was food allergy (31.3%) in accordance with previous studies.^{3-6,14,16} Nuts and cow's milk were the most frequently implicated foods (30.0 and 23.3%, respectively). Our findings were somewhat different from the results of a previous retrospective study from our country²¹ in which beef and nuts followed cow's milk allergy in frequency. Beef allergy was not reported among our patients. The reason for the difference might be that beef allergy is prevalent in the north region of Turkey and most patients in that study came from this region. Although our results are similar to the previous data in literature, generally, the order of allergenic foods varies between countries and studies.^{5,6,24,25,31,34,35} The varying data may be explained by differences in study groups, dietary habits, and hereditary factors. Seafood is not commonly used in our region; thus, only three patients had anaphylaxis because of fish allergy.

In our study, anaphylaxis due to drugs occurred in 27.1% of children. Comparable rates were also reported by Orhan *et al.*²¹ (21%) and Hoffer *et al.*²⁷ (26%). Higher rates are reported from a previous study including both adults and children.⁴ This may be explained by more frequent drug use among adults. In our study antibiotics (57.7%) and nonsteroidal anti-inflammatory drugs (11.5%) were the two most frequent medications causing anaphylaxis in accordance with previous data.^{4,5,8,23} Comparable with the results of previous studies^{3,4,22,24} idiopathic anaphylaxis occurred in 8.3% of patients.

Recurrence of anaphylaxis was most frequently caused by foods, followed by Hymenoptera venom and drugs. Patients and physicians are generally aware of the danger of using the drug causing anaphylaxis and staying away from a defined medication is quite easy. Bee venom allergy is also well known and immunotherapy helps to prevent recurrences. A few of our cases had a mild reaction in their first sting and anaphylaxis after a recurrent exposure. Although reactions to recurrent bee stings are usually not more severe than the previous one there are a few cases such as our patients in the literature.^{36,37} High recurrence rate among patients with food allergy stresses the importance of clear food labeling and of extensive dietetic information.

The low frequency of biphasic reactions we noticed is in contrast to the findings of some studies (19.4–9%).^{38,39} In the study by Ellis *et al.*, 4 of 20 patients with biphasic reactions were children and the other study included only adults. Biphasic reaction rates comparable with our study are reported from two studies conducted among children.^{21,40} It seems that among children, biphasic reactions may be less frequent than adults. Four of five patients with biphasic reactions had a severe reaction at the first attack and other clinical characteristics were similar between patients with and without biphasic reactions.

Atopic diseases were more frequent among children with food-induced anaphylaxis as was reported in previous reports.²¹ In addition, atopic patients had a higher frequency of recurrent anaphylaxis in our study. Therefore, regardless of the causative agent, patients with atopic diseases should be followed carefully for recurrences.

The most frequently used medication to treat anaphylaxis was antihistamines (86.8%), which is comparable with the findings of other surveys.^{4,7,21,22,41} In general, in almost all studies use of adrenaline is less than use of antihistamines and corticosteroids. Although more frequent than previous studies,^{21,22} adrenaline was administered in only 44.4% of our cases and there was no difference between severity groups. These data reveal the need for education to promote the use of epinephrine in the treatment of anaphylaxis.

In conclusion, etiology and clinical features of anaphylaxis in our patients was similar to those of patients in other countries, although bee venom allergy was slightly more common. Treatment of anaphylaxis was found inadequate; and adrenaline is used in only 44.4% of patients. Education for the treatment of this potentially life-threatening state is needed.

REFERENCES

1. Simons FE, Arduzzo LR, Bilo MB, et al. World allergy organization anaphylaxis guidelines: Summary. *J Allergy Clin Immunol* 127:587–593, e581–e522, 2011.

2. Greenberger PA, and Ditto AM. Chapter 24: Anaphylaxis. *Allergy Asthma Proc* 33(suppl 1):S80–S83, 2012.
3. Worm M, Edenharter G, Ru[uml]tjeff F, et al. Symptom profile and risk factors of anaphylaxis in central Europe. *Allergy* 67: 691–698, 2012.
4. Hsin YC, Hsin YC, Huang JL, and Yeh KW. Clinical features of adult and pediatric anaphylaxis in Taiwan. *Asian Pac J Allergy Immunol* 29:307–312, 2011.
5. Tejedor Alonso MA, Moro Moro M, Mugica Garcia MV, et al. Incidence of anaphylaxis in the city of Alcorcon (Spain): A population-based study. *Clin Exp Allergy* 42:578–589, 2012.
6. Peng MM, and Jick H. A population-based study of the incidence, cause, and severity of anaphylaxis in the United Kingdom. *Arch Intern Med* 164:317–319, 2004.
7. Poachanukoon O, and Paopairochanakorn C. Incidence of anaphylaxis in the emergency department: A 1-year study in a university hospital. *Asian Pac J Allergy Immunol* 24:111–116, 2006.
8. Helbling A, Hurni T, Mueller UR, and Pichler WJ. Incidence of anaphylaxis with circulatory symptoms: A study over a 3-year period comprising 940,000 inhabitants of the Swiss Canton Bern. *Clin Exp Allergy* 34:285–290, 2004.
9. Liew WK, Williamson E, and Tang ML. Anaphylaxis fatalities and admissions in Australia. *J Allergy Clin Immunol* 123:434–442, 2009.
10. Yang MS, Lee SH, Kim TW, et al. Epidemiologic and clinical features of anaphylaxis in Korea. *Ann Allergy Asthma Immunol* 100:31–36, 2008.
11. Sole D, Ivancevich JC, Borges MS, et al. Anaphylaxis in Latin America: A report of the online Latin American survey on anaphylaxis (Olasa). *Clinics (Sao Paulo)* 66:943–947, 2011.
12. Grabenhenrich L, Hompes S, Gough H, et al. Implementation of anaphylaxis management guidelines: A register-based study. *PLoS One* 7:e35778, 2012.
13. Rubio M, Bousquet PJ, Gomes E, et al. Results of drug hypersensitivity evaluations in a large group of children and adults. *Clin Exp Allergy* 42:123–130, 2012.
14. Harduar-Morano L, Simon MR, Watkins S, et al. A population-based epidemiologic study of emergency department visits for anaphylaxis in Florida. *J Allergy Clin Immunol* 128:594–600, e591, 2011.
15. Tejedor Alonso MA, Moro MM, Hernandez JE, et al. Incidence of anaphylaxis in hospitalized patients. *Int Arch Allergy Immunol* 156:212–220, 2011.
16. Lieberman P, Camargo CA Jr, Bohlke K, et al. Epidemiology of anaphylaxis: Findings of the American College of Allergy, Asthma and Immunology Epidemiology of Anaphylaxis working group. *Ann Allergy Asthma Immunol* 97:596–602, 2006.
17. Alves B, and Sheikh A. Age specific aetiology of anaphylaxis. *Arch Dis Child* 85:348, 2001.
18. Han Y, Kim J, and Ahn K. Food allergy. *Korean J Pediatr* 55:153–158, 2012.
19. Przybilla B, and Rueff F. Hymenoptera venom allergy. *J Dtsch Dermatol Ges* 8:114–127, 2010.
20. Muraro A, Roberts G, Clark A, et al. The management of anaphylaxis in childhood: Position paper of the European Academy of Allergology and Clinical Immunology. *Allergy* 62:857–871, 2007.
21. Orhan F, Canitez Y, Bakirtas A, et al. Anaphylaxis in Turkish children: A multi-centre, retrospective, case study. *Clin Exp Allergy* 41:1767–1776, 2011.
22. De Swert LF, Bullens D, Raes M, and Dermaux AM. Anaphylaxis in referred pediatric patients: Demographic and clinical features, triggers, and therapeutic approach. *Eur J Pediatr* 167: 1251–1261, 2008.
23. Novembre E, Cianferoni A, Bernardini R, et al. Anaphylaxis in children: Clinical and allergologic features. *Pediatrics* 101:E8, 1998.

24. Mehl A, Wahn U, and Niggemann B. Anaphylactic reactions in children—A questionnaire-based survey in Germany. *Allergy* 60:1440–1445, 2005.
25. Braganza SC, Acworth JP, McKinnon DR, et al. Paediatric emergency department anaphylaxis: Different patterns from adults. *Arch Dis Child* 91:159–163, 2006.
26. de Silva IL, Mehr SS, Tey D, and Tang ML. Paediatric anaphylaxis: A 5 year retrospective review. *Allergy* 63:1071–1076, 2008.
27. Hoffer V, Scheuerman O, Marcus N, et al. Anaphylaxis in Israel: Experience with 92 hospitalized children. *Pediatr Allergy Immunol* 22:172–177, 2011.
28. Dibs SD, and Baker MD. Anaphylaxis in children: A 5-year experience. *Pediatrics* 99:E7, 1997.
29. DeMuth KA, and Fitzpatrick AM. Epinephrine autoinjector availability among children with food allergy. *Allergy Asthma Proc* 32:295–300, 2011.
30. Vetander M, Helander D, Lindquist C, et al. Classification of anaphylaxis and utility of the EAACI Taskforce position paper on anaphylaxis in children. *Pediatr Allergy Immunol* 22:369–373, 2011.
31. Huang F, Chawla K, Jarvinen KM, et al. Anaphylaxis in a New York City pediatric emergency department: Triggers, treatments, and outcomes. *J Allergy Clin Immunol* 129:162–168, e161–e163, 2012.
32. Simons FE. Anaphylaxis, killer allergy: Long-term management in the community. *J Allergy Clin Immunol* 117:367–377, 2006.
33. Cianferoni A, Novembre E, Pucci N, et al. Anaphylaxis: A 7-year follow-up survey of 46 children. *Ann Allergy Asthma Immunol* 92:464–468, 2004.
34. Calvani M, Cardinale F, Martelli A, et al. Risk factors for severe pediatric food anaphylaxis in Italy. *Pediatr Allergy Immunol* 22:813–819, 2011.
35. Amin AJ, and Davis CM. Changes in prevalence and characteristics of IgE-mediated food allergies in children referred to a tertiary care center in 2003 and 2008. *Allergy Asthma Proc* 33:95–101, 2012.
36. Valentine MD, Schuberth KC, Kagey-Sobotka A, et al. The value of immunotherapy with venom in children with allergy to insect stings. *N Engl J Med* 323:1601–1603, 1990.
37. Golden DB, Kagey-Sobotka A, Norman PS, et al. Outcomes of allergy to insect stings in children, with and without venom immunotherapy. *N Engl J Med* 351:668–674, 2004.
38. Ellis AK, and Day JH. Incidence and characteristics of biphasic anaphylaxis: A prospective evaluation of 103 patients. *Ann Allergy Asthma Immunol* 98:64–69, 2007.
39. Lieberman P. Biphasic anaphylactic reactions. *Ann Allergy Asthma Immunol* 95:217–226, 2005.
40. Lee JM, and Greenes DS. Biphasic anaphylactic reactions in pediatrics. *Pediatrics* 106:762–766, 2000.
41. Erkocoglu M, Civelek E, Azkur D, et al. Knowledge and attitudes of primary care physicians regarding food allergy and anaphylaxis in Turkey. *Allergol Immunopathol* 2012. DOI: 10.1016/j.aller.2012.05.004. (Epub ahead of print.) □

Copyright of Allergy & Asthma Proceedings is the property of OceanSide Publications Inc. and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.