

Anaphylaxis in an Emergency Department: A 2-Year Study in a Tertiary-Care Hospital

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SUMMARY The aim of this study was to estimate the incidence of anaphylaxis in the emergency department of a tertiary-care hospital, describe the clinical features and the management of the patients and determine those with mild manifestations. A retrospective study was conducted from 2005 to 2006 using anaphylaxis-related ICD-10 terms. Two different sets of criteria for the diagnosis of anaphylaxis were applied, first the criteria previously accepted by emergency practice, followed by the recent criteria set forth at the 2005 international meeting. Sixty-four patients fulfilled the previous criteria with an average incidence of 52.5 per 100,000 patients per year with a shift towards females in 2006. The most common presentations were cutaneous, followed by respiratory symptoms. Food allergy was the most common cause, especially prawn. After applying the recent criteria, 13 patients (20.4%) were excluded, which reduced the incidence to 42.2 per 100,000 patients per year. Long term follow up is suggested for the possible or mild cases that were re-categorized.

Anaphylaxis is a severe, life-threatening, acute systemic hypersensitivity reaction, often IgE-mediated.¹ There is still no universal agreement on the definition or the criteria for the diagnosis of anaphylaxis, probably due to its dynamic and multifactorial nature. In July 2005, the National Institute of Allergy and Infectious Diseases (NIAID) and the Food Allergy and Anaphylaxis Network (FAAN) of the USA, including other representatives from North America, Europe and Australia proposed a new set of diagnostic criteria.² Since most anaphylaxis patients are first managed by physicians in emergency departments (ED), the diagnostic criteria and management guidelines have to make sense and be useful for them. There was only one study on anaphylaxis patients who visited the ED of a university hospital in Thailand in 2004, which reported an incidence of

223 per 100,000 patients per year³, using the criteria for diagnosis reported by Yocum *et al.*⁴ The purpose of this study was 1) to determine the incidence of anaphylaxis in the patients who visited the ED of Bhumibol Adulyadej Hospital, Bangkok, Thailand, in 2005-2006, 2) to describe the clinical features and management of anaphylaxis, and 3) to compare the diagnosis using the previous criteria in ED practice⁴ with the new criteria derived from the expert meeting in 2005 in order to evaluate the severity of anaphylaxis in the patients, which has not been done before in Thailand.

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MATERIALS AND METHODS

Study population

A retrospective case study of all patients who were diagnosed with anaphylaxis at the Emergency Department (ED) of Bhumibol Adulyadej Hospital, which is a university-affiliated tertiary-care hospital in Bangkok, Thailand, was performed from January 1, 2005 to December 31, 2006. The patients' charts were selected based on the International Classification of Diseases (ICD) version 10, using the discharge diagnosis of anaphylaxis due to the following conditions: adverse food reaction, adverse effect of a correct drug or properly administered medicament, adverse serum effects, and unspecified causes. The medical records were then analyzed by the first author (K.P.) to confirm the diagnosis. Anaphylaxis was defined, using the criteria of Yocum *et al.*,⁴ by the presence of one symptom of generalized mast cell-mediator release such as flushing; localized pruritus or paresthesia of the lips, axilla, hands, or feet; generalized pruritus; urticaria or angioedema; and conjunctivitis or chemosis. In addition to the symptoms of generalized mast cell-mediator release, at least one other system involvement besides the skin was required: 1) respiratory system: dyspnea, wheezing, rhinitis, cough, hoarseness, stridor, aphonia, or cyanosis 2) cardiovascular system: chest tightness, hypotension, dizziness, syncope, tachycardia, bradycardia, arrhythmia, shock, or seizure, and 3) oral and gastrointestinal system: edema of the buccal mucosa, tongue, palate, or oropharynx; nausea, emesis, dysphagia, abdominal cramps, or diarrhea.

Assessment using the new criteria

After we assessed the patient's data by the criteria mentioned above, we did another assessment using the new criteria proposed by the second symposium on the definition and management of anaphylaxis.² By the new criteria, anaphylaxis is highly likely when any one of the following criteria are fulfilled: 1) acute onset of illness (minutes to several hours) with involvement of skin, mucosal tissue, or both (*e.g.* generalized hives, pruritus, or flushing, swollen lips-tongue-uvula) *and at least one of the following*: a) respiratory compromise (*e.g.* dyspnea, wheeze-bronchospasm, stridor, reduced peak expira-

tory flow [PEF], hypoxemia); b) reduced BP (blood pressure) or associated symptoms of end organ dysfunction (*e.g.* hypotonia [collapse], syncope, incontinence); 2) two or more of the following that occur rapidly after exposure to a *likely allergen for that patient*: a) involvement of skin or mucosal tissue (*e.g.* generalized hives, itch-flush, swollen lips-tongue-uvula); b) respiratory compromise (*e.g.* dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia); c) reduced BP or associated symptoms (*e.g.* hypotonia [collapse], syncope, incontinence); d) persistent gastrointestinal symptoms (*e.g.* crampy abdominal pain, vomiting), and 3) reduced BP after exposure to a *known allergen* for that patient (minutes to several hours): a) infants and children: low BP (age specific) or greater than a 30% decrease in systolic BP; b) adults: systolic BP of less than 90 mm Hg or greater than a 30% decrease from that person's base line.

We re-classified our patients who suddenly developed generalized cutaneous symptoms together with other mild symptoms such as gastro-intestinal symptoms, *e.g.* dysphagia, nausea/vomiting, abdominal pain, or mild respiratory symptoms, *e.g.* rhinitis, or hoarseness, which fulfilled the previous criteria but did not fulfill the new criteria, as having a *possible* anaphylaxis or *mild degree* of anaphylaxis. The study was approved by the Ethics Committee of Bhumibol Adulyadej Hospital.

Medical record review

The medical records were reviewed to gather demographic data, *e.g.* age, sex. Other data that were analyzed included place, time of onset after the exposure to the allergens, symptoms, signs, treatment and outcome. Patients were classified as having an allergic history if they had a history of asthma, allergic rhinitis, urticaria, angioedema, food allergy, drug allergy, or eczema.

Statistical analysis

The Statistical Package for the Social Science (SPSS), version 10.0 for Windows was used for all statistical calculations. Descriptive statistics were used; the demographic data and patients' characteristics were reported as percentage and median.

RESULTS

Sixty-four patients, *i.e.* 24 patients in 2005 and 40 patients in 2006, satisfied our inclusion criteria for anaphylaxis. The number of patients visiting the ED in the years 2005 and 2006 were 61,414 and 60,443 respectively, therefore, the incidence of anaphylaxis in the year 2005 was 39.1 per 100,000 patients per year, and in 2006 was 66.2 per 100,000 patients per year. The average incidence was 52.5 per 100,000 patients per year. The demographic data are shown in Table 1. The age range was 0.8-66 years, 50 percent of the patients were children under 15 years of age with 16 cases per year. There was an increase in adult patients, especially females, which increased from 7 to 29 per year, while adult males decreased from 17 to 11. The total male: female ratio in the 2-year period was 1:1.3. A reverse in the male: female ratio, from 2.4:1 in 2005 to 1:2.6 in 2006, was observed.

Only two cases (3.2%) occurred within the ED. Twenty three cases (35%) had symptoms within 30 minutes after exposure to the causative agents. Six patients (6.4%) had recurrent episodes of anaphylaxis. Only one patient had a family history of anaphylaxis (a 4-year old boy with prawn-induced anaphylaxis had a maternal history of sea shell-induced anaphylaxis). Two cases (3.2%) had a biphasic anaphylactic reaction (one adult and one child). One mortality in 2005 was a man with acute gastrointestinal and pulmonary infections. He developed shock with cyanosis 20 minutes after receiving

intravenous ceftriaxone and then had another episode of shock 6 hours after admission. The overall mortality was 1.6%. Admission rate was 50% (32/64), out of which 30 cases were children.

Prevalence of allergic disease

Thirty-seven (57.9%) patients gave a history of allergic diseases. In most cases the allergic diseases in anaphylaxis patients were due to food (21/35; 60.0%), followed by drugs (9/18; 50.0%), and insect stings (3/6; 50.0%). The most prevalent allergic history was allergic rhinitis (29.7%), followed by asthma (21.9%), food allergy (21.9%), eczema (9.4%), urticaria (9.4%), drug allergy (7.8%), and angioedema (3.2%).

Symptoms and signs of anaphylaxis

Among the 64 patients, 62 (96.8%) had cutaneous, 42 (65.5%) respiratory, 30 (46.9%) cardiovascular, and 26 (40.6%) oral and gastrointestinal manifestations. Details and percentage symptoms and signs in 4 target organ systems are shown in Table 2. The two adult patients who did not have cutaneous manifestations were those who received intravenous antibiotic (ceftriaxone) injections in the ED. Both patients did not have any cutaneous manifestations in the course of their hospital admission.

Causative agents

The causes of anaphylaxis were food (56.3%),

Table 1 Demographic data of the patients

	2005	2006	Total
No. of patients	24	40	64
Age range	0.8-64.8	3.3-66	0.8-66
≤ 15 years	16	16	32
> 15 years	8	24	32
Sex			
Male	17	11	28
Female	7	29	36
Male:female ratio	2.4:1	1:2.6	1:1.3
≤ 15 years	3:1	1:1.7	1.3:1
> 15 years	1.7:1	1:3.8	1:2.2

drugs (28.1%), insect stings (9.4%) and unknown (6.2%) (Table 3). We found that shrimp (both fresh-water prawn and sea-water shrimp) were the most common cause of food-induced anaphylaxis. Some uncommon causes such as fresh-water fish, bananas, mushroom and kiwi were reported. A remarkable increase in fried insects, mainly fried grasshoppers and fried crickets, as cause of food-induced anaphylaxis was observed. The incidence rose from 4.2% in 2005 to 15% in 2006. One woman who presented with fried insect-induced anaphylaxis developed shrimp-induced anaphylaxis a few months later. The youngest patient was a 9 month-old boy who had fresh-water fish, Red *Tilapia* (Tabtim fish) induced anaphylaxis. The most common insect stings that caused anaphylaxis were inflicted by hornet/wasp species. One patient had anaphylaxis due to a venomous ant, identified as *Tetraponera rufonigra*.

Twenty-five patients (39%) were referred to allergists after discharge, 22 of which were children. A skin prick test was performed to confirm the diagnosis in 7 cases.

Severity

After applying the new criteria for diagnosing anaphylaxis, we found that 17 cases had cutaneous symptoms together with mild symptoms as follows: abdominal symptoms in 10 cases, rhinitis in 4, hoarseness and dysphagia in 2, and tachycardia in 1 case. Among these, only 4 patients had a previous history of allergy to the causative allergens, which fulfilled criterion 2. The remaining 13 cases did not fulfill the new criteria and were classified as *possible anaphylaxis* or *mild cases*, most of which were food-induced. There was a 20.4% reduction in diagnosed cases from the first round, so the incidence was reduced from 52.5 to 42.2 per 100,000 patients per year by the new definition. The data are shown in Table 4.

Treatment

The medications used to treat anaphylaxis are shown in Table 5. Commonly used medications were corticosteroids (95.3%), followed by H1 antihistamines (92.2%). Epinephrine was given to 48 patients (75.0%). The eighteen patients who did not receive epinephrine were assessed by the physician

Table 2 Symptoms and signs of anaphylaxis in the 64 study patients

Symptoms and signs	Number of patients (%)
Cutaneous	62 (96.8)
Angioedema	44 (68.6)
Urticaria	36 (56.3)
General pruritus	15 (23.4)
Flushing	12 (18.8)
Red eyes	11 (17.2)
Local itch or tingling	6 (9.4)
Respiratory system	42 (65.5)
Dyspnea	24 (37.5)
Wheezing	22 (34.4)
Rhinitis	13 (20.3)
Cough	4 (6.3)
Hoarseness	2 (3.1)
Stridor	1 (1.6)
Cyanosis	1 (1.6)
Cardiovascular system	30 (46.9)
Hypotension	18 (28.1)
Chest tightness	5 (7.8)
Dizziness	7 (10.9)
Shock	1 (1.6)
Oral and gastrointestinal system	26 (40.6)
Abdominal pain	12 (18.8)
Nausea	12 (18.8)
Vomiting	9 (14.1)
Diarrhea	7 (10.9)
Dysphagia	3 (4.7)
Intra-oral edema	1 (1.6)

as having mild symptoms, and had uneventful courses in the ED. One patient with ceftriaxone-induced anaphylaxis received epinephrine after an intravenous fluid load, and was diagnosed with fluid overload and ARDS.

DISCUSSION

The incidence of anaphylaxis is a topic of interest and was investigated by many researchers mainly through retrospective studies. The incidence of anaphylaxis in the ED in this study, which was based on the criteria described by Yocum *et al.*,⁴ increased from 39.1 per 100,000 patients per year in 2005 to 66.2 per 100,000 patients per year in 2006. The numbers were lower than those previously

Table 3 Causes of anaphylaxis in the 64 patients

Cause of anaphylaxis	Number of patients (%)		
	2005	2006	2 years
Food	11 (45.8)	25 (62.5)	36 (56.3)
Shrimp (sea + fresh water)	5	7	12
Fish (sea + fresh water)	2	3	5
Crab	1	2	3
Crab + exercise	0	1	1
Squid	0	3	3
Fried insects	1	6	7
Other	2	3	5
Drug	7 (29.2)	11 (27.5)	18 (28.1)
Antibiotics	2	7	9
NSAID/aspirin	4	4	8
Other	1	0	1
Insect sting	3 (16.7)	3 (7.5)	6 (9.4)
Wasps & hornets	3	2	5
Venomous ants	0	1	1
Unknown	3 (16.7)	1 (2.5)	4 (6.2)

Table 4 Cases that fulfilled the new criteria and percentage of total cases

Cause of anaphylaxis	Number of patients that fulfilled new criteria/total cases (%)		
	2005	2006	2 years
Food	7/11 (63.6)	20/25 (80)	27/36 (75.0)
Drug	5/7 (71.4)	10/11 (90.9)	15/18 (83.3)
Insect sting	3/3 (100)	2/3 (66.6)	5/6 (83.3)
Unknown	3/3 (100)	1/1 (100)	4/4 (100)
Total	17/24 (75.0)	26/40 (65.0)	51/64 (79.6)

reported by Poachanukoon *et al.*³ in Pathumthani, Thailand, in 2004, and by Brown⁵ in Australia during 1998-1999, but were higher than those of Sheikh⁶ in the UK during 1991-1995. The difference in the incidence of anaphylaxis in this study compared to the previous report might be due to the dissimilarity of the patient groups who visited the 2 hospitals. For example, Bhumibol Adulyadej Hospital is a referral center for traffic accidents, so patients who have milder symptoms might visit clinics or nearby hospitals instead of our busy ED, which might explain why we observed 40.6% of gastrointestinal symptoms, compared to 69% in the study of Poachanu-

Table 5 Medication used to treat anaphylaxis

Medication	Number of patients (%)
Corticosteroids	61 (95.3)
H1 blocker antihistamine	59 (92.2)
H2 blocker antihistamine	51 (79.7)
Epinephrine	48 (75.0)
Intravenous fluids	34 (53.1)
Inhaled β-agonist	11 (17.2)
Inotropic drugs	2 (3.1)

koon and Paopairochanakorn.³ The average incidence of 52.5 per 100,000 patients per year in this study was close to the 55.45 per 100,000 admitted patients at Siriraj Hospital, reported by Jirapongsananurak *et al.*⁷ in 2004. In the two-year period of our study, we had 16 pediatric patients each year, or 24.6 per 100,000 ED patients per year. A steady incidence in pediatric patients was also found in the study of a health maintenance organization, who found no increase in the incidence of anaphylaxis in children during their study period from 1991 to 1997 (10.5 episodes per 100,000 person-year).⁸ Since our study was only a 2-year study, the trend of the incidence of anaphylaxis in children should be further observed. Contrary to the children, the number of adult patients rose from 8 to 24 patients per year, especially female patients, resulting in an adult male:female ratio of 1:2.2, while the pediatric male:female was 1.3:1, and the total male:female ratio was 1:1.3. An increase in female anaphylaxis patients of child-bearing age was observed by Sheikh in the UK,⁶ and in adult in-patients by Jirapongsananurak *et al.*⁷ The age range in this study was from 9 months to 66 years old, in agreement with other studies.^{3,7}

After applying the new diagnostic criteria, 13 of the 64 patients (20.4%) were re-classified as possible anaphylaxis or mild cases. The ambiguous symptoms of these 13 cases that questioned the diagnosis of anaphylaxis were oral and gastrointestinal symptoms; mild respiratory symptoms such as rhinitis and hoarseness; and tachycardia. These patients had generalized cutaneous reactions after exposure to an agent that never provoked any reaction previously. They would need to consult with an allergist for further investigations and register for follow up. Another problem for making a clear diagnosis was the lack of objective evidence in some patients who presented with chest tightness or dyspnea. Careful monitoring of PEF, vital signs, and symptom changes before and after epinephrine as recommended by the expert committee, may solve this problem.²

One male patient with an underlying infectious disease died of drug-induced anaphylaxis. He developed ARDS after an intravenous fluid load, which was administered before injecting epinephrine at the ED. This finding stresses the importance of an

early administration of epinephrine as primary drug for the management of anaphylaxis. The mortality was 1.6% which was in agreement with a previous ED study by Poachanukoon *et al.*,³ but was higher than the report on in-patients by Jirapongsananurak *et al.*⁷ Delayed diagnosis and delayed epinephrine administration in ED patients might be the most important factors leading to death.

An allergic history was observed in 57.9% of patients, which was close to the number observed by Poachanukoon *et al.*³ and Jirapongsananurak *et al.*⁷ We found that patients with food-induced anaphylaxis had the highest incidence of allergic history. We also found an increased occurrence of allergic history in drug-induced and insect sting anaphylaxis patients compared to the general population.⁹ Since the size of our study was rather small the findings regarding drug-induced anaphylaxis would need further confirmation.

Cutaneous manifestations were observed in 96.8% of the patients in agreement with other studies.^{3,10} Two patients who did not have cutaneous manifestations presented with hypotension and shock after intravenous cephalosporin. Shock without cutaneous manifestation was a common manifestation in penicillin-induced anaphylaxis. The reduction of benzathine penicillin usage resulted in a marked decrease of the incidence of penicillin-induced anaphylaxis.¹⁰ Other symptoms were in agreement with a previous report,¹⁰ except we found less laryngeal edema. Only 3.2% of the patients in this study had a biphasic reaction, which was close to the 4.9%,⁷ 5.3%,¹¹ and 6%,¹² but lower than the 15%,³ and 20%¹³ reported elsewhere. Two cases with biphasic reaction had a history of delayed epinephrine administration, in agreement with the study by Lee *et al.*¹²

Our youngest patient was a 9 month-old boy with no allergic history, and definite anaphylactic symptoms due to a fresh-water fish, Red *Tilapia*, to which he was exposed only a few times previously. This might be due to an unusual sensitization *via* maternal diet during pregnancy and breast-feeding.

In our study, food was the most important cause of anaphylaxis in both adult and children. The leading cause was shrimp; both fresh-water prawn

and sea-water shrimp. We did not find wheat, cow milk, or egg as causes of anaphylaxis in this study, unlike previous reports.^{7,3,14} The reason may be due a small number of pediatric patients in our study and the duration of study was not long enough to cover every possible cause. Anaphylaxis to fried insects though (fried grasshoppers and crickets) was observed in 7 patients (one children and 6 adults), which was more than in a previous study.⁷ Fried insects are nowadays a favorite snack in our country. Although the patterns of food-induced anaphylaxis in Asian countries have something in common, there are also variations; for example we did not find birds' nest-induced anaphylaxis like in Singapore.¹⁵ These findings differed from western studies. Sea food was the most common cause of anaphylaxis in Asian studies, with only a few sporadic reports of peanuts or other nuts as causes of anaphylaxis. These findings may suggest the importance of infant feeding practices, cooking procedures, and priming of T cells during early life, as suggested by a previous study.¹⁶

Insect stings were observed in 9.4% of the patients, similar to a previous study by Jirapongsananurak *et al.*⁷ Wasps and hornets were the most common cause of stings in our study in agreement with Pochnukoon *et al.*³ The most important hornets in Thailand are *Vespa affinis* which build aerial nests and *Vespa tropica* which build underground nests. Temperate hornets (*Dolichovespula* spp.), and yellow jackets (*Vespula* spp.) do not exist in our country.

Corticosteroids and H1 antihistamines were the two most common drugs used by physicians (95.5% and 92.2% respectively). Intramuscular epinephrine was used in 75.0%, similar to a previous study in our country,⁷ but slightly lower than in another study.³ The absence of skin manifestations resulted in the delayed administration of epinephrine in one patient who had drug-induced hypotension.

Since our study was a retrospective study, there were limitations in confirming the diagnosis. The allergist consultation rate was low in our institute, further education for ED physicians about anaphylaxis may help to achieve more co-operation and improve the accuracy of the diagnosis and quality of management. As 20.4% of our cases might be ex-

cluded because of mild symptoms, we think that those patients still need education about a possible future chance of anaphylaxis and should commit to a long term follow up. Further studies on the allergenicity of different food items and food additives, as well as on the effect of feeding patterns in children and eating habits of adults on food allergy/anaphylaxis might answer some open questions.

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