

Repeat epinephrine treatments for food-related allergic reactions that present to the emergency department

Aleena Banerji, M.D.,¹ Susan A. Rudders, M.D.,² Blanka Corel, M.D.,³ Alisha M. Garth, M.D.,³ Sunday Clark, M.P.H., Sc.D.,⁴ and Carlos A. Camargo, Jr., M.D., Dr.P.H.^{1,3}

ABSTRACT

To date, there are sparse data on epinephrine treatment for food-related anaphylaxis in adults. We sought to establish the frequency of more than one epinephrine treatment for adult patients who present with food-related anaphylaxis to the emergency department (ED). We performed a chart review, at two academic centers, of all adults presenting to the ED for food allergy (ICD9CM codes 693.1, 995.0, 995.1, 995.3, 995.7, 995.60–995.69, 558.3, 692.5, and 708.X) between January 1, 2001 and December 31, 2006. We focused on causative foods; treatments, including the number of epinephrine treatments given before and during the ED visit; and disposition. Through random sampling and appropriate weighting, the 486 reviewed cases represented a study cohort of 1286 patients. The median age was 36 years and the cohort was 62% women. Shellfish (23%), peanuts (12%), tree nuts (14%), and fish (14%) provoked the allergic reaction most commonly. Most patients (62%; 95% confidence interval [CI], 57–68%) met criteria for food-related anaphylaxis. In the ED, anaphylaxis patients received epinephrine (18%), antihistamines (91%), corticosteroids (81%), and inhaled albuterol (19%). Overall, 17% (95% CI, 9–25%) of patients with food-related anaphylaxis given epinephrine received >1 dose over the course of their reaction. Among anaphylaxis patients admitted to the hospital, only 10% included anaphylaxis in the discharge diagnosis. At ED discharge (82% of patients), 18% were referred to an allergist and 39% were prescribed self-injectable epinephrine. Among ED patients with food-related anaphylaxis treated with epinephrine, 17% were given >1 dose. This study supports the recommendation that patients at risk for food-related anaphylaxis should carry 2 doses of epinephrine.

(Allergy Asthma Proc 31:308–316, 2010; doi: 10.2500/aap.2010.31.3375)

Key words: Adult, allergy, anaphylaxis, antihistamines, atopy, emergency department, epinephrine, food allergy, risk factors, steroids, treatment

Food allergies are estimated to affect ~4% of the U.S. population and recent studies have shown an increasing prevalence rate.^{1,2} Patients with food allergies are at risk for food-related anaphylaxis, a life-threatening acute allergic reaction. Epinephrine has been shown to be the most effective treatment for anaphylaxis.³ Prompt treatment with epinephrine has been shown not only to decrease hospital admission rates for anaphylaxis but also decrease fatalities from food-related anaphylaxis.^{4–7} Despite this knowledge, food-related anaphylaxis continues to be inadequately treated.^{8,9}

Recently, based on limited data,¹⁰ a recommendation was developed for patients at risk for anaphylaxis to carry 2 doses of epinephrine.¹¹ This led us to perform a

small pilot study looking at the need for more than one epinephrine treatment in food-related anaphylaxis. We reviewed all cases of food-related allergic reactions presenting to the Massachusetts General Hospital Emergency Department (ED) over a 1-year period of time from 1999 to 2000. We found that ~16% of patients with food-related anaphylaxis were treated with more than one epinephrine treatment.¹² Given the possible implications of these findings to patients at risk for food-related anaphylaxis, we expanded our pilot study to evaluate the need for more than one epinephrine treatment in a much larger population.

METHODS

Study Design

We performed a chart review at two academic hospitals in Boston (Massachusetts General Hospital and Brigham and Women's Hospital) of all adult patients presenting to the ED over a 6-year period (January 1, 2001 to December 31, 2006) with food-related allergic reactions. We have previously studied International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes used to identify patients presenting to the ED for food-related allergic reactions and used codes that would comprehensively identify all cases of food

From the ¹Division of Rheumatology, Allergy and Immunology, Department of Medicine, and ³Department of Emergency Medicine, Massachusetts General Hospital, Boston, Massachusetts, ²Division of Allergy and Immunology, Children's Hospital Boston, Boston, Massachusetts, and ⁴Division of General Internal Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania

C. Camargo has consulted for Dey (Napa, California); this project was partly supported by an investigator-initiated research grant to C. Camargo from Dey

Address correspondence and reprint requests to Aleena Banerji, M.D., Division of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, 55 Fruit Street, Cox 201, Boston, MA 02114

E-mail address: abanerji@partners.org

Copyright © 2010, OceanSide Publications, Inc., U.S.A.

Table 1 Demographic characteristics and medical history of adults presenting to the emergency department with a food-related allergic reaction (proportion [95% CI])

	Overall (n = 1286)	No Anaphylaxis (n = 484)	Anaphylaxis* (n = 802)	p Value
Demographic characteristics				
Age, median (SE), yr	36 (0.7)	36 (1.2)	36 (0.9)	0.68
Female	62 (57–67)	61 (53–70)	62 (55–70)	0.83
Race/ethnicity				<0.001
White	55 (50–60)	47 (39–56)	60 (53–66)	
Black	19 (15–23)	21 (15–28)	17 (12–23)	
Hispanic	13 (10–17)	11 (6–15)	15 (10–19)	
Asian	4 (2–7)	4 (1–8)	5 (2–7)	
Other race	8 (5–11)	16 (9–23)	4 (1–6)	
Medical history				
Known allergy to offending allergen	51 (46–57)	45 (36–53)	55 (48–62)	0.08
Known allergic problems	61 (56–67)	53 (45–62)	66 (60–72)	0.02
Prior allergic reactions to other sources	74 (67–81)	72 (61–83)	75 (67–83)	0.66
Asthma	43 (36–51)	39 (27–51)	46 (36–55)	0.42
Hay fever	9 (5–14)	9 (1–17)	10 (4–15)	0.88
Atopic dermatitis	3 (1–5)	2 (0–6)	3 (1–6)	0.68
Hives	1 (0–2)	NC#	NC#	—
Angioedema	0.1 (0–0.3)	NC#	0 (0–0)	—
Other allergic problems	0.1 (0–0.3)	0	NC#	—
Patient owns EpiPen	27 (21–32)	16 (9–23)	33 (25–41)	0.002

*Anaphylaxis defined as allergic reaction involving more than one organ system or hypotension (systolic blood pressure of <100 mmHg).

#NC, noncalculable; when the number of observations was <30, robust estimates could not be produced.

CI = confidence interval.

allergy presenting to the ED.¹³ The codes used were 995.60 (anaphylactic shock due to unspecified food), 995.61–995.69 (anaphylactic shock due to specified food), 995.0 (other anaphylactic shock), 693.1 (dermatitis due to food), 995.7 (adverse food reaction, not otherwise classified), 558.3 (allergic gastroenteritis), and 692.5 (contact dermatitis due to food). In addition, random samplings of the codes 995.3 (allergy, unspecified), 995.1 (angioedema), and 708.X (urticaria) were reviewed to identify cases of food-related allergic reactions within these more nonspecific allergy codes. All charts were reviewed by physicians and then reviewed by an allergist for both accuracy and internal consistency.

Data Collection

Standardized data abstraction forms were used to collect data on patient demographics, medical and atopic history, food allergy triggers, clinical presentation, pre-ED and ED treatment (with a focus on epinephrine treatment), discharge diagnosis, and discharge instructions (including allergy referrals and prescriptions for epinephrine autoinjector).

Definitions

A food-related acute allergic reaction was defined as an acute episode of IgE-mediated symptoms in which the onset was temporally related to a known or suspected food allergen. Anaphylaxis was defined similar to diagnostic criteria established by the second symposium of the National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network.³ Specifically, food-related anaphylaxis was defined as an acute allergic reaction involving two or more organ systems after exposure to a likely food allergen or hypotension alone after exposure to a known food allergen. For consistency with our earlier work,¹³ hypotension was defined as a systolic blood pressure of <100 mmHg for adults in an emergency situation. We examined the impact of using <90 mmHg as the threshold and it did not materially alter the findings (data not shown).

Statistical Analysis

We used a stratified sampling method to reflect the population of patients treated in the ED within each ICD-9 code. Sample weights were assigned to account

Table 2 Presentation and clinical course of adults presenting to the emergency department (ED) with a food-related allergic reaction (proportion [95% CI])

Presentation and Clinical Course	Overall (<i>n</i> = 1286)	No Anaphylaxis (<i>n</i> = 484)	Anaphylaxis* (<i>n</i> = 802)	<i>p</i> Value
Arrive to ED by ambulance	34 (28–40)	20 (13–28)	44 (36–52)	<0.001
Time since exposure				0.19
<1 hr	31 (25–37)	30 (19–40)	32 (24–40)	
1–3 hr	37 (31–44)	34 (25–44)	39 (31–47)	
4–6 hr	12 (8–17)	9 (4–14)	14 (8–21)	
7–12 hr	3 (1–5)	4 (0–9)	2 (0–4)	
>12 hr	17 (11–22)	23 (14–32)	13 (6–20)	
Location of exposure				0.37
Home	32 (27–38)	32 (23–45)	31 (24–39)	
School	2 (0.2–4)	1 (0.3–3)	3 (0–6)	
Work	6 (3–10)	5 (0–10)	7 (2–12)	
Restaurant	52 (45–59)	48 (37–59)	54 (45–63)	
Other	7 (2–11)	11 (3–20)	4 (0–9)	
Specific food trigger causing current reaction				
Shellfish	23 (18–27)	26 (18–34)	21 (15–27)	0.32
Peanuts	12 (9–15)	6 (4–9)	15 (10–20)	0.001
Tree nuts	14 (11–18)	12 (8–17)	15 (11–20)	0.39
Seeds	3 (1–5)	5 (0–10)	1 (1–2)	0.03
Fruits and vegetables	14 (10–18)	16 (9–22)	13 (8–18)	0.54
Fish	14 (10–18)	23 (15–31)	9 (5–13)	0.001
Milk products	5 (3–8)	4 (2–5)	6 (3–10)	0.15
Eggs	2 (0.3–5)	1 (0–2)	4 (0.2–7)	0.06
Wheat	0.3 (0–1)	1 (0–2)	0	0.06
Other Food	28 (23–33)	22 (15–29)	32 (25–39)	0.047
Signs and symptoms				
Skin rash	65 (60–70)	62 (54–71)	67 (60–73)	0.41
Itching	57 (51–62)	57 (49–66)	56 (49–63)	0.81
Swelling	45 (39–50)	41 (32–50)	47 (40–54)	0.32
Angioedema	12 (9–15)	12 (6–17)	13 (9–17)	0.72
Trouble swallowing	20 (16–24)	4 (1–6)	30 (23–36)	<0.001
Trouble breathing/shortness of breath	39 (33–44)	6 (1–11)	58 (51–65)	<0.001
Wheezing	14 (10–17)	2 (1–3)	21 (15–26)	<0.001
Hoarse voice	7 (4–10)	0.2 (0.2–0.2)	11 (6–15)	<0.001
Stridor	2 (0.2–3)	0	2 (0.4–4)	0.07
Nausea/vomiting	11 (7–15)	2 (0.1–3)	17 (11–22)	<0.001
Abdominal pain/cramps	5 (3–8)	1 (0–3)	8 (3–12)	0.003
Diarrhea	4 (1–7)	0	6 (2–10)	0.02
Abdominal tenderness	1 (0–2)	0	1 (0–3)	0.34
Dizziness/fainting	4 (2–7)	0	7 (3–11)	0.01
Altered mental status	1 (0–3)	0	2 (0–5)	0.13
Admitted to hospital	18 (15–22)	13 (8–18)	22 (17–26)	0.02
Among discharged to home				
Prescribed self-injectable epinephrine	39 (32–45)	30 (21–39)	44 (35–53)	0.03
Referred to allergist	18 (13–23)	13 (6–20)	21 (13–28)	0.13
Instructions to avoid offending allergen	68 (62–73)	59 (50–69)	73 (66–81)	0.02
Discharge diagnosis included term “anaphylaxis”	3 (1–5)	0.2 (0–0.5)	5 (2–8)	<0.001

Table 2 Continued

Presentation and Clinical Course	Overall (n = 1286)	No Anaphylaxis (n = 484)	Anaphylaxis* (n = 802)	p Value
Among admitted to hospital				
Prescribed self-injectable epinephrine	59 (48–69)	41 (17–66)	64 (50–78)	0.17
Referred to allergist	35 (22–48)	39 (12–66)	33 (21–46)	0.68
Instructions to avoid offending allergen	61 (50–71)	73 (5–91)	57 (44–70)	0.21
Discharge diagnosis included term “anaphylaxis”	8 (4–12)	2 (0–5)	10 (5–15)	0.04
Antihistamines prescribed at discharge	86 (82–90)	81 (74–88)	88 (84–93)	0.07
H ₁ -blockers prescribed	95 (92–98)	97 (94–100)	94 (90–98)	0.20
H ₂ -blockers prescribed	52 (46–59)	57 (47–66)	50 (42–58)	0.29
Steroids prescribed at discharge	64 (58–69)	51 (42–59)	71 (65–78)	<0.001

*Anaphylaxis defined as allergic reaction involving more than one organ systems or hypotension (systolic blood pressure of <100 mmHg).

CI = confidence interval.

for unequal probabilities of selection, oversampling, and nonresponse. The weights were applied for analyses using the survey module in STATA 10.0 (StataCorp, College Station, TX). Data are expressed as mean $\pm$ standard error (SE) and proportion, with 95% confidence interval (CI). Comparisons between non-anaphylaxis and anaphylaxis groups were evaluated using chi-square tests. Because of the relatively small number of patients with the main outcome (*i.e.*, receipt of more than one epinephrine treatment), multivariable analysis was performed using unweighted visit numbers to explore risk factors for repeat epinephrine use. A two-sided $p < 0.05$ was considered statistically significant.

RESULTS

Over the 6-year period, we reviewed charts for 486 patient visits for food-related allergic reactions presenting to the ED. With appropriate weighting, this represented a study cohort of 1286 patients. Most of these cases (62%; 95% CI, 57–68%) met criteria for food-related anaphylaxis. No fatalities were identified.

Demographics

The median age was 36 (SE, 0.7 years) years (Table 1). There was a female predominance (62%) and most patients were white (55%). The median age and gender distribution was similar between anaphylaxis and non-anaphylaxis patients. However, there was a slightly increased percentage of white patients in the anaphylaxis group (60%) compared with the nonanaphylaxis group (47%).

Atopic History

Among all patients, 61% had a prior atopic history with 43% reporting a history of asthma. The frequency of asthma was similar between anaphylaxis and nonanaphylaxis patients. Approximately one-half of the patients had a known allergy to the offending allergen, but only 27% of patients reported owning self-injectable epinephrine. Patients with food-related anaphylaxis were more likely to own self-injectable epinephrine when compared with nonanaphylaxis patients. Similarly, patients with food-related anaphylaxis treated with epinephrine were more likely to own self-injectable epinephrine than anaphylaxis patients not treated with epinephrine.

Food Allergy Triggers

Overall, the most common triggers of a food-related allergic reaction were shellfish (23%), peanuts (12%), tree nuts (14%), and fish (14%). Similarly, shellfish (21%), peanuts (15%), and tree nuts (15%) were the most common triggers of food-related anaphylaxis. Peanut exposure was associated with an increased risk of food-related anaphylaxis (Table 2) and these patients were more likely to be treated with epinephrine than no epinephrine (Table 3). The specific food trigger was not associated with receiving more than one epinephrine treatment (data not shown).

Patients reported exposure to the offending agent most commonly at a restaurant (52%) or at home (32%). Patients who received epinephrine were much less likely to be at home immediately before coming to the ED compared with patients that did not receive any epinephrine (Table 3).

Table 3 Overview of adults presenting to the emergency department (ED) with a food-related anaphylaxis,* according to any treatment with epinephrine (proportion [95% CI])

	No epinephrine (n = 179)	Epinephrine (n = 116)	p Value
Medical history			
Known allergy to offending allergen	54	66	0.047
Patient owns EpiPen	19	56	<0.001
Presentation and clinical course			
Arrive to ED by ambulance	27	46	0.002
Time since exposure			0.006
<1 hr	29	40	
1–3 hr	43	45	
4–6 hr	11	14	
7–12 hr	3	0	
>12 hr	14	1	
Onset of symptoms			0.049
<1 hr	36	50	
1–3 hr	38	38	
>3 hr	26	12	
Location of exposure			0.04
Home	37	32	
School	1	4	
Work	2	13	
Restaurant	55	49	
Other	4	3	
Location immediately before ED arrival			0.01
Home	53	35	
School	1	4	
Work	2	11	
Restaurant	34	34	
Doctor office/clinic	5	13	
Other	5	2	
Specific food trigger causing current reaction			
Shellfish	21	20	0.77
Peanuts	13	27	0.003
Tree nuts	18	17	0.89
Seeds	4	3	0.54
Fruits and vegetables	12	13	0.76
Fish	8	9	0.94
Milk products	4	6	0.55
Eggs	2	1	0.56
Admitted	19	46	<0.001

*Anaphylaxis defined as allergic reaction involving more than one organ system or hypotension (systolic blood pressure of <100 mmHg).

SD = standard deviation;

CI = confidence interval.

Clinical Presentation

Only one-third of adults presented to the ED within 1 hour after exposure to the food allergen. Eighty percent presented to the ED within 6 hours after exposure. Adults with food-related anaphylaxis that were treated with epinephrine presented more quickly—i.e., 85%

presented to the ED within 3 hours of exposure to the food allergen.

Anaphylaxis patients presented to the ED by ambulance more frequently than nonanaphylaxis patients (44% versus 20%; $p < 0.001$). Similarly, anaphylaxis patients treated with epinephrine presented to the ED

Table 4 Treatment of adults presenting to the emergency department (ED) with a food-related acute allergic reaction (proportion [95% CI])

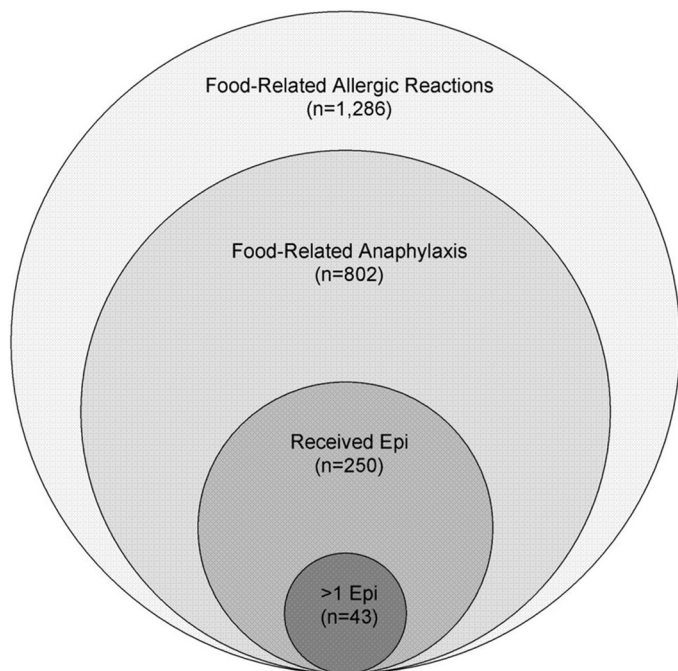
	Overall (n = 486)	No Anaphylaxis (n = 191)	Anaphylaxis* (n = 295)	p Value
Pre-ED treatments (<3 hr before triage)	47 (42–53)	43 (34–51)	50 (43–57)	0.18
Epinephrine	28 (21–35)	17 (7–28)	33 (24–43)	0.04
Benadryl	84 (78–91)	90 (81–99)	82 (73–90)	0.23
Other antihistamines	8 (4–13)	11 (1–21)	7 (2–11)	0.34
Steroids	9 (4–13)	6 (2–11)	10 (3–17)	0.38
i.v. fluids	5 (1–9)	1 (0.1–2)	7 (0.3–13)	0.001
Inhaled β -agonists	7 (3–12)	3 (0.2–7)	9 (2–16)	0.08
Oxygen	0.5 (0.1–1)	0.4 (0–1)	0.5 (0–1)	0.98
Number of pre-ED epinephrine				0.01
0 doses	87 (83–90)	93 (88–97)	83 (78–88)	
1 dose	13 (10–17)	7 (3–12)	17 (12–2)	
2+ doses	0.1 (0.05–0.1)	0	0.1 (0–0.3)	
No. of epinephrine doses given in ED				<0.001
0 doses	87 (84–90)	95 (92–98)	82 (77–87)	
1 dose	11 (8–15)	5 (2–8)	15 (11–20)	
2+ doses	1 (0.5–2)	0	2 (1–4)	
No. of epinephrine doses given in ED among patients receiving epinephrine in the ED				—
1 dose	89 (82–96)	100	87 (79–95)	
2+ doses	11 (4–18)	0	13 (5–21)	
Total no. of epinephrine doses given				<0.001
0 doses	76 (72–80)	88 (83–93)	69 (62–75)	
1 dose	21 (17–25)	12 (7–17)	26 (20–32)	
2+ doses	3 (2–5)	0	5 (2–8)	
Total no. of epinephrine doses given among patients receiving any epinephrine				—
1 dose	86 (79–93)	100	83 (75–91)	
2+ doses	14 (7–21)	0	17 (9–25)	
ED antihistamines given	89 (86–92)	87 (82–91)	91 (87–95)	0.20
Benadryl	82 (77–86)	82 (75–90)	81 (75–87)	0.82
Other H ₁ -blockers	2 (1–3)	1 (1–2)	2 (0.4–4)	0.46
H ₂ -blockers	83 (78–87)	75 (67–84)	87 (82–92)	0.02
ED steroids given				<0.001
Prednisone	30 (25–35)	35 (27–43)	27 (21–33)	
Methylprednisolone (Solu-Medrol)	41 (36–47)	21 (14–28)	53 (46–60)	
Other	1 (0.2–1)	1 (0–2)	1 (0.5–1)	
None	28 (23–33)	43 (34–51)	19 (13–25)	
Inhaled β -agonists given	13 (9–16)	3 (1–4)	19 (14–24)	<0.001
Oxygen	10 (7–13)	4 (2–6)	14 (9–19)	<0.001
i.v. Fluids given	53 (46–60)	52 (38–65)	54 (45–62)	0.81

Anaphylaxis defined as allergic reaction involving more than one organ system or hypotension (systolic blood pressure of <100 mmHg).

CI = confidence interval.

by ambulance more frequently than anaphylaxis patients not treated with epinephrine (46% versus 27%; $p = 0.002$).

From a clinical perspective, patients with anaphylaxis most commonly had symptoms of skin rash (67%), itching (56%), swelling (47%), shortness of breath (58%), and



- Among all patients with food-related allergic reactions, 3% received >1 dose of epinephrine.
- Among all patients with food-related anaphylaxis, 5% received >1 dose of epinephrine.
- Among all patients who received epinephrine for food-related anaphylaxis, 17% received >1 dose of epinephrine.

Figure 1. Percentages of adults receiving >1 dose of epinephrine within different population groups.

trouble swallowing (30%). Adults with food-related anaphylaxis treated with epinephrine presented more frequently with itching, swelling, shortness of breath, wheezing, and vomiting compared with anaphylaxis patients that did not receive epinephrine (data not shown).

Pre-ED and ED Course

Before arrival at the ED, 47% of all patients received treatment (Table 4). Patients who received pre-ED epinephrine most frequently administered their own self-injectable epinephrine device (58%). In the ED, patients received epinephrine (13%), antihistamines (89%), corticosteroids (72%), and inhaled albuterol (13%). Epinephrine was most frequently given subcutaneously (91%). In the ED, among all patients with food-related allergic reactions treated with epinephrine, 11% received more than one epinephrine treatment. Over the course of their reaction, 14% (95% CI, 7–18%) of patients given epinephrine in the ED received >1 dose.

Approximately, one-third of patients with food-related anaphylaxis were treated with any epinephrine during the course of their reaction. Overall, 17% (95% CI, 9–25%) of patients with food-related anaphylaxis given epinephrine received more than one treatment over the course of their reaction (Fig. 1). On average, for patients with anaphylaxis, 2nd doses of epinephrine were administered 73 minutes (SE 29) after the 1st dose. Multivariate analysis did not find any statistically significant factors associated with more than one epinephrine treatment among adults presenting to the ED with food-related anaphylaxis.

Disposition

The majority of patients were discharged home from the ED (82%). Among those discharged home, only 18% were referred to an allergist and 39% were prescribed self-injectable epinephrine (Table 2). These percentages were slightly higher among patients admitted to the hospital with 35% being referred to an allergist and 59% being prescribed self-injectable epinephrine. Adults with food-related anaphylaxis were more likely to be admitted to the hospital compared with nonanaphylaxis patients (Table 2). Patients with food-related anaphylaxis treated with any epinephrine were also more likely to be admitted to the hospital compared with anaphylaxis patients not treated with epinephrine (Table 3).

Among all patients with food-related anaphylaxis discharged home directly from the ED, only 5% were assigned a diagnosis on discharge from the ED that included the term anaphylaxis. Even among all patients with food-related anaphylaxis admitted to the hospital, only 8% were assigned a diagnosis on discharge from the ED that included the term anaphylaxis.

DISCUSSION

Approximately 100–150 deaths/year are attributed to food-related anaphylaxis.^{2,5} Despite the life-threatening nature of anaphylaxis, there are sparse data on the management and outcome of this disease. This is largely because of highly variable definitions and diverse clinical presentations that can make anaphylaxis difficult to diagnose and treat optimally. However,

epinephrine has been shown to be the most effective treatment for anaphylaxis.³ To our knowledge, this 6-year study is the largest study of adult ED patients with food-related anaphylaxis with specific reference to epinephrine treatments. Our study indicates that food-related anaphylaxis continues to be underrecognized and inadequately treated. In the ED, the majority of patients were administered epinephrine subcutaneously despite current guidelines indicating that the optimal route of administration is intramuscular.³ Less than 10% of patients meeting clinical criteria for anaphylaxis were assigned a diagnosis on discharge from the ED that included the term anaphylaxis. Only 31% of patients presenting with food-related anaphylaxis received any epinephrine treatment.

Because of significant concerns, based on limited data,¹⁰ a recommendation was previously developed for patients at risk for anaphylaxis to carry 2 doses of epinephrine.¹¹ In our population, among ED patients with a food-related allergic reaction treated with epinephrine, 14% were given more than one epinephrine treatment. In anaphylaxis patients treated with epinephrine, 17% were given more than one epinephrine treatment during the course of their reaction. Prior studies similarly showed that 16–35% of patients with anaphylaxis required treatment with >1 dose of epinephrine.^{10,12,14,15} However, we should be cautious in our interpretation of the data because when considering all adult patients who presented to the ED for food-related anaphylaxis, only 5% received more than one epinephrine treatment (Fig. 1). Therefore, although all food-related allergic reactions did not require epinephrine treatment, a significant number of patients treated with epinephrine received more than one epinephrine treatment.

The risk factors for requiring more than one epinephrine treatment remain unclear. This could partially be attributed to the small number of subjects ($n = 43$; Fig. 1) treated with >1 dose of epinephrine. Accordingly, until the risk factors for requiring more than one epinephrine treatment are better understood, it may be advisable for patients at risk for food-related anaphylaxis to carry multiple doses of epinephrine, especially in situations where the risk is perceived to be higher. For example, if food-allergic patients will be in locations where access to care is less readily available¹⁶ or eating at a restaurant or buffet where the food ingredients are less clear, they should be encouraged to carry multiple doses of epinephrine.

Peanuts, tree nuts, shellfish, and fish were the most common food allergy triggers seen in patients presenting to the ED for food-related allergic reactions. They accounted for 63% of all reactions in patients with anaphylaxis treated with epinephrine. Specifically, peanut allergy was associated with increased risk of anaphylaxis and need for epinephrine treat-

ment in the ED. This is consistent with data suggesting that peanut, tree nut, and shellfish allergies are associated with more severe food-related allergic reactions.^{2,17} Interestingly, fruits and vegetables, foods typically believed to have low allergenicity, accounted for 14% of all reactions. Although most physicians are able to recognize the dangers of nuts and shellfish, we must not forget that less allergenic foods can also cause severe allergic reactions.

The majority of patients was discharged home from the ED and did not require hospital admission, but despite being given the diagnosis and treatment for a food-related anaphylactic reaction, only 18% were referred to an allergist for further evaluation and 39% were prescribed self-injectable epinephrine. Our data are similar to recently published data showing that among patients presenting to the ED for anaphylaxis only 31% of patients were given allergy referrals and 36% of patients were prescribed self-injectable epinephrine on discharge.¹⁸ These data suggest that we are missing an opportunity to provide appropriate education and follow-up management in these patients. Several reasons have been previously cited¹⁸ for the low rate of prescriptions for self-injectable epinephrine and referral to an allergist including (1) lack of proper documentation, (2) failure to properly diagnose anaphylaxis, and (3) lack of a universally accepted definition for anaphylaxis. When symptoms are not life-threatening, physicians are less likely to diagnose anaphylaxis.⁸ Although significant improvements have been made, additional work is still needed for EDs to comply with national guidelines for the management of patients presenting with food-associated anaphylactic reactions.

A potential limitation of our study is reliance on the medical record and the possibility that the documentation of medication use was incomplete. Because of the design of our study, we were unable to complete a formal allergy evaluation to the identified offending allergen, but patients did present to the ED with a history and physical exam consistent with a food-related allergic reaction. In addition, limiting our review to the ED may overestimate the percentage of patients receiving epinephrine because less severe allergic reactions may be managed at home or in a primary care setting. However, studies have shown the majority of anaphylaxis cases are treated in the ED; therefore, it would follow logically that ED visits would accurately reflect rates of repeat epinephrine use in cases of food-related anaphylaxis.¹⁹ It was also not possible to determine whether the repeat epinephrine doses used during the course of the reaction were truly required. We have therefore chosen to describe epinephrine treatments as having been received rather than being required. Finally, our data may not be nationally representative because the two hospitals evaluated were located in an urban, academic setting.

Although, the risk factors for treatment with multiple doses of epinephrine remain unclear, our data contributes to the growing literature showing that some patients with food-related anaphylaxis require more than one epinephrine treatment. Among adult ED patients with a food-related anaphylaxis treated with epinephrine, 17% were given >1 dose. Our data further support the recommendation that individuals at risk for food-related anaphylaxis should carry 2 doses of epinephrine, especially when there is no easy access to emergency care.

REFERENCES

1. Sampson HA. Update on food allergy. *J Allergy Clin Immunol* 113:805–819, 2004.
2. Munoz-Furlong A, and Weiss CC. Characteristics of food-allergic patients placing them at risk for a fatal anaphylactic episode. *Curr Allergy Asthma Rep* 9:57–63, 2009.
3. Sampson HA, Munoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: Summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *Ann Emerg Med* 47:373–380, 2006.
4. Bock SA, Munoz-Furlong A, and Sampson HA. Further fatalities caused by anaphylactic reactions to food, 2001–2006. *J Allergy Clin Immunol* 119:1016–1018, 2007.
5. Bock SA, Munoz-Furlong A, and Sampson HA. Fatalities due to anaphylactic reactions to foods. *J Allergy Clin Immunol* 107:191–193, 2001.
6. Pumphrey RS. Lessons for management of anaphylaxis from a study of fatal reactions. *Clin Exp Allergy* 30:1144–1150, 2000.
7. Pumphrey RS, and Gowland MH. Further fatal allergic reactions to food in the United Kingdom, 1999–2006. *J Allergy Clin Immunol* 119(4):1018–1019, 2007.
8. Klein JS, Yocum MW. Underreporting of anaphylaxis in a community emergency room. *J Allergy Clin Immunol* 95:637–638, 1995.
9. Sheikh A, Ten Broek V, Brown SG, and Simons FE. H1-antihistamines for the treatment of anaphylaxis: Cochrane systematic review. *Allergy* 62:830–837, 2007.
10. Uguz A, Lack G, Pumphrey R, et al. Allergic reactions in the community: A questionnaire survey of members of the anaphylaxis campaign. *Clin Exp Allergy* 35:746–750, 2005.
11. Kelso JM. A second dose of epinephrine for anaphylaxis: How often needed and how to carry. *J Allergy Clin Immunol* 117:464–465, 2006.
12. Oren E, Banerji A, Clark S, and Camargo CA Jr. Food-induced anaphylaxis and repeated epinephrine treatments. *Ann Allergy Asthma Immunol* 99:429–432, 2007.
13. Clark S, Gaeta TJ, Kamarthi GS, and Camargo CA. ICD-9-CM coding of emergency department visits for food and insect sting allergy. *Ann Epidemiol* 16:696–700, 2006.
14. Jarvinen KM, Sicherer SH, Sampson HA, and Nowak-Wegrzyn A. Use of multiple doses of epinephrine in food-induced anaphylaxis in children. *J Allergy Clin Immunol* 122:133–138, 2008.
15. Korenblat P, Lundie MJ, Dankner RE, and Day JH. A retrospective study of epinephrine administration for anaphylaxis: How many doses are needed? *Allergy Asthma Proc* 20:383–386, 1999.
16. Carr BG, Branas CC, Metlay JP, et al. Access to emergency care in the United States. *Ann Emerg Med* 54:261–269, 2009.
17. Kemp AS. EpiPen epidemic: Suggestions for rational prescribing in childhood food allergy. *J Paediatr Child Health* 39:372–375, 2003.
18. Campbell RL, Luke A, Weaver AL, et al. Prescriptions for self-injectable epinephrine and follow-up referral in emergency department patients presenting with anaphylaxis. *Ann Allergy Asthma Immunol* 101:631–636, 2008.
19. Branum AM, and Lukacs SL. Food allergy among U.S. children: Trends in prevalence and hospitalizations. NCHS Data Brief, No. 10, October 2008. Available online at www.cdc.gov/nchs/data/databriefs/db10.pdf; last accessed January 2010. □

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.