

Evaluation of Anaphylaxis Management in a Pediatric Emergency Department

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Objective: In 2006, the National Institute of Allergy and Infectious Disease established evidence-based treatment guidelines for anaphylaxis. The purpose of our study was to evaluate provider adherence to guidelines-based management for anaphylaxis in a tertiary care pediatric emergency department (ED).

Methods: Retrospective chart review was conducted of patients (0–18 years) presenting to the Arkansas Children Hospital ED from 2004 to 2011 for the treatment of anaphylaxis using *International Classification of Diseases, Ninth Edition*, codes. Multiple characteristics including demographics, clinical features, allergen source, and anaphylaxis management were collected. Fisher exact or χ^2 tests were used to compare proportion of patients treated with intramuscular (IM) epinephrine in the preguideline versus postguideline period. Relative risk (RR) statistics were computed to estimate the ratio of patients who received self-injectable epinephrine prescription and allergy follow-up in the preguideline and postguideline groups.

Results: A total of 187 patients (median [range] age, 7[1–18] years; 67% male; 48% African American) were evaluated. Food (44%) and hymenoptera stings (22%) were commonly described culprit allergens, whereas 29% had no identifiable allergen. Only 47% (n = 87) received epinephrine in the ED and 31% (n = 27) via the preferred IM route. Comparing postguideline (n = 126) versus preguideline (n = 61) periods demonstrated increase in the usage of the IM route (46% postguideline vs 6% preguideline; risk ratio (RR), 7.64; 95% confidence interval [CI], 2.04–46.0; $P < 0.001$). Overall, 61% (n = 115) of the patients received self-injectable epinephrine upon discharge, and there were no significant differences between the groups (64% postguideline vs 56% preguideline, $P = 0.30$). Postguideline patients were more likely to receive a prescription compared with preguideline patients (64% postguideline vs 56% preguideline; RR, 1.15; 95% CI, 0.89–1.55; $P = 0.30$). Only 45% (n = 85) received an allergy referral. Postguideline patients were more likely to receive an allergy referral than preguideline patients (48% postguideline vs 41% preguideline; RR, 1.16; 95% CI, 0.81–1.73; $P = 0.40$).

Conclusions: Provider use of IM epinephrine has improved since anaphylaxis guidelines were published. However, more provider education is needed to improve overall adherence of guidelines in a tertiary care pediatric ED.

Key Words: anaphylaxis, epinephrine, intramuscular, guidelines

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Anaphylaxis is a severe, systemic allergic reaction that occurs suddenly after contact with an allergy-causing substance. Anaphylaxis in the pediatric emergency department (ED) is most commonly associated with food allergies, with other common causes including latex, drugs, and insect stings.¹ In the United

States, the prevalence of food allergy among children younger than 18 years increased 18% from 1997 to 2007.² Peanut allergy has doubled in children (1997–2002) with fatal food anaphylaxis most often caused by exposure to peanuts/tree nuts.³ Other allergens such as hymenoptera stings can cause life-threatening reactions in 0.4% to 0.8% of children.⁴

Based on these statistics and a lack of universal agreement on a definition for the diagnosis of anaphylaxis, the second symposium on the definition and management of anaphylaxis was held by the National Institute of Allergy and Infectious Disease (NIAID) and the Food Allergy and Anaphylaxis Network. In 2006, clinical criteria were established by these groups with evidence-based guidelines for the diagnosis and management of anaphylaxis.⁵

The guidelines published that anaphylaxis was highly likely when any 1 of the following 3 criteria is fulfilled⁵:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, and swollen lips-tongue-uvula) and at least one of the following:
 - a. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced peak expiratory flow, and hypoxemia)
 - b. Reduced blood pressure (BP) or associated symptoms of end-organ dysfunction (eg, hypotonia [collapse], syncope, and incontinence)
2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):
 - a. Involvement of the skin-mucosal tissue (eg, generalized hives, itch-flush, and swollen lips-tongue-uvula)
 - b. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced peak expiratory flow, and hypoxemia)
 - c. Reduced BP or associated symptoms (eg, hypotonia [collapse], syncope, and incontinence)
 - d. Persistent gastrointestinal symptoms (eg, crampy abdominal pain and vomiting)
3. Reduced BP after exposure to known allergen for that patient (minutes to several hours):
 - a. Infants and children: low systolic BP (age-specific) or greater than 30% decrease in systolic BP
 - b. Adults: systolic BP < 90 mm Hg or a > 30% decrease from the person's baseline

The NIAID guidelines also recommend a standardized management approach to anaphylaxis including the use of intramuscular (IM) epinephrine as first-line therapy, educational instruction at discharge, prescription for self-injectable epinephrine, and follow-up with a specialist.⁵ Intramuscular epinephrine is considered the criterion standard for treatment, because it is known to provide faster and higher peak of plasma concentrations compared with the subcutaneous (SQ) route.⁶

Since the establishment of these guidelines, few studies have sought to review the subsequent changes in a pediatric ED's

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management of anaphylaxis. Similar studies have been performed in Europe using a protocol established by the European Academy of Allergy.⁷ The purpose of the current investigation was to assess the adherence to the guidelines in the ED. We also examined the incidence and timing of epinephrine usage as recommended by the guidelines. Furthermore, we examined the likelihood that patients presenting with anaphylaxis were provided with self-injectable epinephrine prescription, patient education, and follow-up evaluation.

EXPERIMENTAL DESIGN AND METHOD

We conducted a retrospective chart review of patients (age, 0–18 years) presenting to the Arkansas Children's Hospital ED from 2004 to 2011 for the treatment of anaphylaxis. The study was approved by the University of Arkansas for Medical Sciences Institutional Review Board.

Subjects

Patients (children aged 0–18 years) who presented to the Arkansas Children's Hospital ED between January 2004 and January 2006 (preguideline period) and those from July 2007 and July 2011 (postguideline period) for the treatment of anaphylaxis were identified. Subjects were identified using *International Classification of Diseases, Ninth Edition, (ICD-9)* codes for anaphylaxis including the following: anaphylaxis, overdose or wrong substance given or taken (977.9); anaphylaxis after sting(s) (989.5); anaphylaxis, latex (989.82); anaphylaxis, adverse effect of correct medicinal substance properly administered (995.0); urticaria with angioedema (995.1); anaphylaxis, allergy, unspecified (995.3); anaphylaxis, allergy, unspecified food (995.60); anaphylaxis, allergy, peanuts (995.61); anaphylaxis, allergy, crustaceans (995.62); anaphylaxis, allergy, fruits, vegetables (995.63); anaphylaxis, allergy, tree nuts, seeds (995.64); anaphylaxis, allergy, fish (995.65); anaphylaxis, allergy, additives (995.66); anaphylaxis, allergy, milk products (995.67); anaphylaxis, allergy, eggs (995.68); anaphylactic reaction due to other specified food (995.69); anaphylactic shock, immunization, serum (999.4); and allergic, hypersensitivity, drugs (995.2). Patients were not actively recruited. The data collected were from existing records only.

Data Collection

The following variables were collected via chart review: patient demographics (age, sex, race/ethnicity), initial presentation/symptoms, allergen source, medical history, amount/route and timing of epinephrine, other treatment modalities used (intravenous fluids, antihistamines, oxygen, albuterol, pressors, steroids), patient education, referral to the primary care physician and/or allergy/immunology specialist, self-injectable epinephrine prescription and user education, disposition (home vs admit), and occurrence of biphasic reaction. Data for this project were queried from MEDITECH (Medical Information Technology Inc), deidentified, and extracted to a secure Microsoft access database specifically designed for the project.

Statistical Analysis

Data were imported into Statistical Analysis Software SAS (Cary NC, v 9.2) and R v 3.1.1 for data analyses. Differences between postguideline and preguideline groups were assessed using proportions and relative risk (RR) ratios with 95% confidence intervals (CIs). Statistical significance was assessed using a 0.05 significance level and determined on the basis of Fisher exact test or Pearson χ^2 test for outcome measures and categorical patient characteristics (sex, race, financial class, and epinephrine before arrival). Wilcoxon-Mann-Whitney tests were used to compare continuous-type patient characteristics (age and weight).

RESULTS

A total of 1500 potential subjects were initially identified; 445 records from the 2004 to 2006 preguideline period and 1055 records from the 2007 to 2011 postguideline period. Of the records from the preguideline period, 61 cases were included; 126 cases were included from the postguideline period. Records were excluded for the following reasons: incorrect ICD-9 coding, case did not meet the multisystem anaphylaxis criteria, or case had incomplete documentation.

Demographics

The median (range) age was 7 (1–18) years in the combined cases (N = 187). A majority of the patients were male (67%), 48% were African American, and at least more than 92% were insured (Table 1).

TABLE 1. Demographic Characteristics by Study Period

	Preguideline (n = 61)	Postguideline (n = 126)	Combined (N = 187)	P
Age, y	5, 9, 13, 9(5)	3, 6, 11, 7 (5)	3, 7, 12, 8(5)	0.02*
Sex, male, n (%)	39 (64)	86 (68)	125 (67)	0.60†
Race, n (%)				0.70†
White	25 (41)	57 (45)	82 (44)	
African American	30 (49)	60 (48)	90 (48)	
Others	6 (10)	9 (7)	15 (8)	
Weight, kg*	16, 30, 55, 36(24)	12, 20, 40, 30(23)	13, 22, 46, 32(24)	0.08*
Financial class, n (%)				1.0†
Private	22 (36)	47 (37)	69 (37)	
Medicaid	35 (57)	71 (56)	106 (57)	
Self-pay	4 (7)	8 (6)	12 (6)	
EPI before arrival, n (%)‡	6 (10)	22 (17)	28 (15)	0.30†

*Wilcoxon-Mann-Whitney test.

†Fisher exact test for count data test.

‡One participant has a missing observation for this variable in the preintervention period.

a, b, c, x (s) indicate the lower quartile, median, the upper quartile c for continuous-type measures, and mean (SD), respectively.

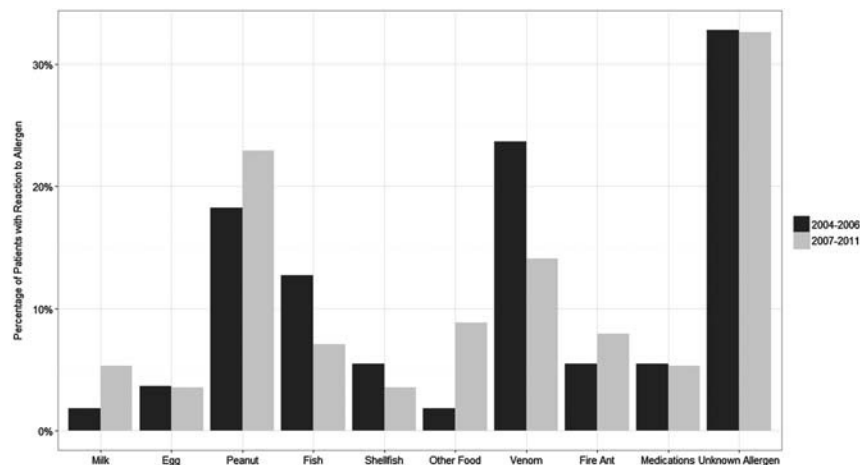


FIGURE 1. Inciting allergens per intervention period. Percentage of patients with reaction to the allergen preanaphylaxis and postanaphylaxis guidelines recommendations.

Medical History

Overall, there was a significant overlap in medical history of the 2 study groups. Of all evaluated, 13% had a previous episode of anaphylaxis, with 50% having had a history of allergies. A history of asthma was documented in 33% of patients. A greater proportion of patients in the postguideline group had reported having a self-injectable epinephrine prescription when compared with the preguideline group (25% postguideline vs 15% preguideline, $P = 0.10$), although this was not statistically significant.

Inciting Allergens

Overall, food was the most commonly identified allergen causing anaphylaxis at 44%, with the highest proportion of food-induced anaphylaxis caused by peanut exposure (19%). The next most common food group included fish/shellfish at 12% (Fig. 1). Overall, 29% of patients had no identifiable allergen, a finding consistent in the postguideline and preguideline groups (29% postguideline vs 30% preguideline). To analyze cases of fire ant anaphylaxis in our pediatric population, we separated this group from traditional hymenoptera venom stings (eg, wasps, yellow jackets, and hornets). The overall frequency of anaphylaxis to venom stings was 16%. The overall frequency of anaphylaxis to fire ants was 6%, and there was no significant difference in the rate of this allergen between the 2 study groups. Anaphylaxis caused by medication was noted at an overall amount of 5%.

Clinical Features

The most common clinical features present in both groups included skin involvement (98%) and angioedema of lips, mouth, and throat (81%). Clinical features of skin involvement included but were not limited to symptoms such as documented hives, urticaria, and rashes. Neurological symptoms such as dizziness and syncope were rare in our patient population (10% postguideline vs 7% preguideline, $P = 0.50$). Respiratory symptoms (79% postguideline vs 92% preguideline; RR, 0.86; 95% CI, 0.79–0.99; $P = 0.02$) and gastrointestinal symptoms (29% postguideline vs 57% preguideline; RR, 0.50; 95% CI, 0.35–0.73; $P < 0.001$) were significantly higher than the preguideline group. There were no significant differences in the rates of reactions for cutaneous and respiratory systems.

Pre-Emergency Department Management

A majority of patients (91%) in both groups arrived to the ED via private vehicle with only 9% arriving via ambulance. Thirty-eight percent had already received a dose of an antihistamine at home/school or in the ambulance. A much smaller portion, 15% ($n = 28$ overall), received self-injectable epinephrine before arrival (at home or in ambulance). This was not statistically significant in the postguideline (17%) and preguideline (10%) groups ($P = 0.30$).

Emergency Department Management

Of those charts reviewed, 187 patients met the NIAID guidelines criteria for a diagnosis of anaphylaxis. Of those patients, a majority in each group (93% postguideline and 92% preguideline) received treatment with an antihistamine in the ED (Table 2). Similarly, most patients (75% postguideline and 73% preguideline) received treatment with corticosteroid medications. A much smaller proportion of patients received treatment with intravenous fluids with the postguideline patients having received more (19%

TABLE 2. Emergency Department Management

	Preguideline (n = 61)	Postguideline (n = 126)	P
ED treatment epinephrine	35 (57)	52 (41)	0.04*
ED treatment epinephrine IM route*	2 (6)	25 (46)	<0.001*
Route†			
SQ	94 (31)	29 (54)	
Antihistamine‡	55 (92)	117 (93)	0.80§
Corticosteroid	46 (75)	92 (73)	0.70§
Albuterol	14 (23)	16 (13)	0.07§

Data are presented as n (%).
*Fisher exact test.
†ED treatment epinephrine route only available for the patients treated with epinephrine ($n = 87$).
‡One patient has a missing observation in the preintervention period.
§Pearson χ^2 test used for count data test.

postguideline vs 5% preguideline; RR, 3.87; 95% CI, 1.19–16.0; $P = 0.01$). The postguideline group had a smaller proportion of patients who received albuterol nebulizer medication (13% postguideline vs 23% preguideline, $P = 0.07$). There was no significance between the 2 groups with regard to the ED use of epinephrine for the treatment of anaphylaxis. The overall usage of epinephrine was 47% ($n = 87$). Postguideline group had significantly less usage in the route of epinephrine administration between the 2 groups (41% postguideline vs 57% preguideline; RR, 0.72; 95% CI, 0.53–0.99; $P = 0.04$). Comparing preguideline ($n = 61$) versus postguideline ($n = 126$) periods demonstrated an increase in the usage of the IM route (46% postguideline vs 6% preguideline; RR, 7.64; 95% CI, 2.04–46.0; $P < 0.001$). However, a larger majority of patients (69%) received epinephrine via the SQ route for either period (Table 2). After epinephrine dosing, none of the patients were admitted to the hospital, and the majority were observed in the ED for more than 4 hours from the last dose of epinephrine.

Discharge Management

Of 187 patients, 61% ($n = 115$) received a self-injectable epinephrine upon discharge (64% postguideline vs 56% preguideline, $P = 0.30$, Table 3). Postguideline patients were 15% more likely to receive a self-injectable epinephrine prescription. However, this was not considered a significant difference (RR, 1.15; 95% CI, 0.89–1.55). Only 45% ($n = 85$) received an allergy referral. Postguideline group had a higher proportion (48% vs 41%) receiving an allergy referral compared with the preguideline group (RR, 1.16; 95% CI, 0.81–1.73; $P = 0.40$). A similar proportion of patients in both groups received a prescription for corticosteroids upon discharge (58% postguideline vs 57% preguideline, $P = 0.90$). Only 6% of cases reviewed were indicative of having a significant biphasic reaction, as defined as returning to the ED within 72 hours of discharge because of recurrence of symptoms. Of those patients presenting with a biphasic reaction, 33% had a history of allergies and 16% had a previous episode of anaphylaxis. The most common trigger involved was an unknown allergen in 58% of the cases. Eighty-three percent of patients with a biphasic reaction had been treated with epinephrine for their initial phase of anaphylaxis. Ninety-two percent of them had received corticosteroids.

Limitations

This study is limited by its retrospective nature. Documentation was not standardized and limited by the physician who had

seen the patient. Incorrect coding by medical staff was also a limiting factor. A majority of the patients who met clinical criteria for anaphylaxis were actually coded as allergic reaction. In addition, we only looked at a single institution's management of anaphylaxis without comparison with other facilities.

DISCUSSION

The purpose of the current study was to assess the adherence to anaphylaxis guideline diagnosis and management in a tertiary care pediatric ED. Although a majority of the evidence base related to anaphylaxis is published in allergy specialty journals, the ED and its physicians are the frontline for its treatment. Using the criteria established by the NIAID guidelines, charts were reviewed to assess compliance with guidelines-based management.⁵ Incorrect ICD-9 coding by staff, incorrect discharge diagnosis by physicians, and dependence on physician documentation likely affected the chart review for the study. A 2012 review of pediatric patients in the ED demonstrated that a majority that met criteria for anaphylaxis were actually coded as an allergic reaction.⁸ In the preguideline group in our study, only 20% of the patients were accurately given the discharge diagnosis of anaphylaxis. The remaining patients, although they fulfilled the criteria for anaphylaxis, were coded as an allergic reaction. By separating preguideline and postguideline era, we were able to compare and contrast the changes in ED anaphylaxis management and determine which areas needed improvement and continuing physician education.

Multiple studies have shown that the most common causes of anaphylaxis are foods, hymenoptera stings (venom), and medication.⁹ Peanuts, tree nuts, fish, and shellfish are the most common food anaphylaxis triggers in the United States and Europe.¹⁰ Consistent with this, most anaphylaxis reactions in our study were caused by food sources, with peanuts accounting for the largest group (19%). To our knowledge, this is one of the first studies to look at the occurrence of anaphylaxis secondary to fire ants in a pediatric population. Individuals living in fire ant endemic regions have a 30% to 60% chance of being stung each year, with anaphylactic reactions in adults reported to range from 0.6% to 16% of those stung.¹¹ In our population, the overall incidence of anaphylaxis to fire ants was reported to be 6%, with no statistically significant difference between the 2 periods. Overall, a large proportion of anaphylaxis trigger source was recorded as unknown allergen, which may have been impacted by incomplete documentation or lack of family knowledge of the source.

The frequency of anaphylaxis was higher in male patients, as seen in other studies.¹² Consistent with previous reports, we found that African American children had higher rates of anaphylaxis as compared with children of other races.¹³ Unlike other studies that have shown an overall increase in the occurrence of allergies and anaphylaxis,¹² our study demonstrated that there was no overall statistical significance in patients presenting with previous episode of anaphylaxis for the study group periods (13% postguideline vs 11% preguideline). Surprisingly, there was also no statistical significance among patients who had a home self-injectable epinephrine for the study period (25% postguideline vs 15% preguideline). Although awareness and education of anaphylaxis have increased through the years among caregivers, the number of patients' actually documenting home epinephrine availability and its use has remained significantly low in our patient population.

The spectrum of symptoms associated with anaphylaxis is variable. Our data correlate with another study that demonstrated that most patients experience cutaneous symptoms (98%).⁶ Neurological symptoms such as dizziness and syncope were rare in our patient population (10% postguideline vs 7% preguideline). Respiratory symptoms (79% postguideline vs 92% preguideline)

TABLE 3. Emergency Department Discharge Management

	Preguideline (n = 61)	Postguideline (n = 126)	P
Prescription for self-injectable epinephrine	34 (56)	81 (64)	0.30*
Allergist referral	25 (41)	60 (48)	0.40*
Prescription for corticosteroids	35 (57)	73 (58)	0.90†
Prescription for antihistamine‡	51 (84)	118 (94)	0.03†

Data are presented as n (%).

*Fisher exact test.

†Pearson χ^2 test used for count data test.

‡One patient has a missing observation in the preintervention period.

and gastrointestinal symptoms (29% postguideline vs 57% pre-guideline) were much more common. None of our patients presented with cardiovascular symptoms such as cardiovascular collapse, documented hypotension, and cardiac arrest.

In terms of ED management of anaphylaxis, some interesting conclusions can be made from our study. Although epinephrine is the recommended first-line treatment for anaphylaxis, the publication of the universal guidelines has not significantly changed how anaphylaxis was managed in our ED. Our results were similar to other recent studies that have shown a consistently high usage of antihistamines and corticosteroids for management and an overall low-use of epinephrine.¹⁴ Antihistamines are slower in onset of action than epinephrine and should be considered as a second-line treatment for anaphylaxis.⁵ Corticosteroids are also not recommended for acute management of anaphylaxis because of their slow onset of action, and the use of corticosteroids to prevent biphasic reactions has shown to be inconclusive.¹⁵

The anaphylaxis guidelines recommend that epinephrine be given by the preferred IM route in the anterior lateral thigh.⁵ Delaying administration of epinephrine has been associated with increased reaction severity, a greater likelihood of biphasic reactions, and an increase risk of fatality.^{15,16} The IM route of delivery has been shown to be superior to the SQ route in achieving faster and higher peak plasma concentrations. In a randomized controlled clinical pharmacology study conducted at baseline in children at risk of anaphylaxis, the mean time to peak epinephrine levels was 8 minutes after IM injection from self-injectable epinephrine versus 34 minutes after SQ epinephrine injection.¹⁷ The overall usage of epinephrine (41% postguideline vs 57% pre-guideline) in our ED is remarkably low at 47% (n = 87) although it is a uniquely life-saving drug. Fear of serious adverse effects is a commonly cited concern with epinephrine and probably contributes to its underusage for anaphylaxis. Since the publication of the guidelines, there has been an increase in the usage of IM epinephrine in our ED, but overall, a majority of patients in both periods were given SQ epinephrine, although multiple studies have demonstrated its decreased efficacy. Because of the retrospective nature of the study, it is difficult to establish the reasons why a majority of patients received SQ versus IM epinephrine. One reason might be that epinephrine ampules (prefilled syringes) are more readily available within our ED rather than self-injectable epinephrine. The establishment of a standardized protocol and the increased availability of self-injectable epinephrine within the ED may help in increasing the usage of IM epinephrine. The availability of more user-friendly self-injectable epinephrine within our ED might also improve provider knowledge concerning epinephrine and its role in anaphylaxis management.

Biphasic reactions are delayed reactions that can develop up to 72 hours after the initial reaction. Our overall result of 6% was consistent with a review done by Lee and Greenes in 2000.¹⁸ Compared with the overall usage of epinephrine, a much larger percentage of patients (83%) with a biphasic reaction had been treated with epinephrine for their initial phase of anaphylaxis. No patients had more severe biphasic reactions than those in the initial phase. Our data do not suggest that steroids prevent biphasic reactions, because the rate of steroid use was relatively higher in patients with (92%) and without these (73%) reactions. No specific clinical risk factors (previous history of anaphylaxis etc.) helped identify patients who would have biphasic reactions. In addition, there was no statistical significance difference in the type of allergenic trigger between patients with or without biphasic reactions. To monitor for the risk of a biphasic reaction, the guidelines recommend the observation of the postanaphylactic patient for 4 to 6 hours in the ED.⁵ They do recommend longer stays for patients with reactive airway disease because of an increased risk of

fatality. A majority of our patients, per ED documentation, stayed in the ED for longer than 4 hours postepinephrine dose.

It is interesting to note that no significant changes were made in terms of self-injectable epinephrine prescription at discharge and allergist referral. The guidelines recommend a 3-step process for outpatient follow-up and management: self-injectable epinephrine prescription, patient education, and follow-up evaluation.⁵ The results in our study were consistent with a recent study that showed that fewer than 58% of patients were prescribed home self-injectable epinephrine.¹⁴ More physician education and an established ED protocol are required to improve patient education and follow-up after ED discharge.

CONCLUSIONS

In conclusion, it seems that provider education concerning the management and diagnosis of anaphylaxis needs to be improved. Starting with improved education for trainees and faculty concerning the guidelines may be helpful. An anaphylaxis and allergic reaction order set is being developed at our ED. Future studies evaluating its effectiveness are needed to determine whether strides have been made in the treatment of anaphylaxis. We can conclude that overall provider use of IM epinephrine in our ED has improved since anaphylaxis guidelines were published, but more work is needed to maximize optimal epinephrine delivery. In general, more provider education is needed to improve overall adherence of guidelines in a tertiary care pediatric ED.

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