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Pediatric Anaphylaxis Management in the Prehospital Setting

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Abstract

Purpose—Anaphylaxis is a life-threatening systemic allergic reaction that occurs after contact with an allergy-causing substance. Timely administration of intramuscular epinephrine is the treatment of choice for controlling symptoms and decreasing fatalities. Our purpose was to investigate the prehospital management of anaphylaxis among patients receiving care in an urban tertiary care pediatric emergency department (PED).

Methods—We performed a retrospective chart review from May, 2008 to January, 2010 of patients 18 years or younger who received care in the PED for anaphylaxis. Data were extracted by one investigator and included demographic information, patient symptoms, past medical history, medications administered (including route and provider), and final disposition.

Results—We reviewed 218 cases of anaphylaxis in 202 children. Mean age of patients was 7.4 years; 56% of patients were male. Two hundred and fourteen (98%) manifested symptoms in the skin/mucosal system, 68% had respiratory symptoms, 44% had gastrointestinal symptoms, and 2% had hypotension. Sixty-seven percent had a previous history of allergic reaction and 38% had a history of asthma. Seventy-six percent of the patients presented with anaphylaxis to food products, 8% to medications, 1% to stings, and 16% to unknown allergens. Reactions occurred at home or with family members 87% of the time, and at school 12% of the time. Only 36% of the patients who met criteria for anaphylaxis had epinephrine administered by emergency medical services (EMS). Among 26 patients with anaphylactic reactions at school, 69% received epinephrine by the school nurse. Of the 117 patients with known allergies who were with their parents at the time of anaphylactic reaction, 41% received epinephrine. Thirteen patients were seen by a physician prior to coming to the PED; all received epinephrine at the physician's office. In total, epinephrine was given to 41% (89) of the 218 cases prior to coming to the PED.

Conclusions—Our evaluation revealed low rates of epinephrine administration by EMS providers and parents/patients. Education about anaphylaxis is imperative to encourage earlier administration of epinephrine.

Keywords

Anaphylaxis; Prehospital care; Pediatric Emergency Department; Emergency Medical Services; Pediatrics; Nurses

Introduction

Anaphylaxis is a life-threatening systemic allergic reaction most commonly involving the cutaneous/mucosal, respiratory, cardiovascular, and gastrointestinal systems that occurs after contact with an allergy-causing substance.¹ It requires rapid assessment, diagnosis, and treatment. Anaphylaxis is a common problem in the United States with an overall population incidence reported as 21 per 100,000 person-years.² Estimates of incidence of pediatric anaphylaxis are variable and elusive due to insufficient pediatric studies, lack of standardized International Classification of Diseases (ICD) coding, and difficulty with consensus regarding the definition of anaphylaxis.

Multiple studies have shown that timely administration of intramuscular epinephrine is the treatment of choice for controlling symptoms of anaphylaxis, preventing biphasic reactions, maintaining blood pressure, and preventing fatalities.⁴⁻⁹ Additionally, The National Association of EMS Physicians (NAEMSP) issued a position statement in 2011 recommending that all emergency medicine services (EMS) providers carry and administer epinephrine for the treatment of anaphylaxis.¹⁰ Despite this, previous studies show variable and insufficient use of epinephrine in children and adults by EMS providers, nurses, and adolescents or parents prior to emergency department (ED) arrival.¹¹⁻¹⁸ Retrospective evaluations of patients with anaphylaxis presenting to PEDs with anaphylaxis revealed low rates of epinephrine administration, with only 24–27% of patients receiving epinephrine prior to PED arrival with an additional 33–52% receiving epinephrine in the PED.^{19,20} No previous studies have reported the frequency of epinephrine administration by parents and different types of outpatient providers, such as school nurses, physicians, and EMS personnel.^{19,20}

The primary purpose of this study was to evaluate the rates of prehospital epinephrine administration to children with anaphylaxis by different types of individuals and determine which patient factors were associated with prehospital administration of epinephrine. Additionally, we wanted to compare the rates of hospitalization between patients who received epinephrine in the prehospital setting and those who received epinephrine in the PED.

Methods

A retrospective chart review was performed for patients with a diagnosis of anaphylaxis seen in the PED at Yale-New Haven Children's Hospital, urban, academic tertiary care center with an annual ED census of 34,000 patients located in New Haven, CT.

Patients between the ages of 0–18 years seen in the PED between May 1, 2008 and January 31, 2010 with ICD, Ninth Revision (ICD-9) codes for allergic reaction (995.3, V15.01, V15.03), urticaria (708, 708.0, 708.1, 708.9), anaphylaxis (995.0, 995.6, 995.4, 995.69, 995.4), angioedema (995.1), and drug allergy (995.27) were identified as potential subjects. Scanned ED charts were then reviewed by the principal investigator (G.T.) for eligibility. Pediatric patients were included in the study if they met the consensus criteria for anaphylaxis based on the 2006 Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network Symposium (Table 1), or if they were given a final documented diagnosis of anaphylaxis by the attending pediatric emergency medicine physician. Patients were excluded if they were transferred from an outside hospital or were treated in the adult ED. When anaphylaxis classification was indeterminate, a second investigator (M.L.) evaluated the chart and a decision was made by consensus between the two investigators. This involved cases in which epinephrine was given, but the patient was

given a final diagnosis of allergic reaction and not anaphylaxis. For example, a patient with throat tightness and tongue swelling who received epinephrine but was diagnosed with allergic reaction was not considered by our team to meet criteria for anaphylaxis because he or she only had skin/mucosal symptoms according to the 2006 criteria. When possible, EMS information that was missing was obtained from the appropriate EMS agency.

Twenty-two police, volunteer and career fire department, municipal ambulance, and commercial ambulance companies are located in the greater New Haven area and are directed by a single medical oversight authority, the Yale-New Haven Sponsor Hospital Program. All paramedics receive continuing education on a variety of topics including pediatric anaphylaxis, and there is a clinical protocol in place for management of anaphylaxis in children. The protocol, used by the majority of the EMS services in the greater New Haven area, starts with establishing intravenous access and administering fluids while continuing assessment and resuscitation. The protocol then recommends treatment of severe respiratory distress and acute bronchospasm with nebulized albuterol and diphenhydramine, and intramuscular epinephrine for patients with severe cardiopulmonary compromise.

Using a standardized data collection worksheet, clinical and demographic variables including age, sex, symptoms, transport by EMS, duration of transport, allergen type, history of asthma or allergy, patient location during initial allergic reaction, medications given by EMS, parents, or school nurse prior to arrival to the PED, medications given in the PED, and final disposition were recorded. Symptoms were later grouped by system according to the 2006 consensus guidelines described earlier. Descriptive data including frequencies, means, standard deviations, and ranges were calculated. We then sought to determine if the demographic and historical variables or variables related to the current episode were associated with outpatient administration of epinephrine. Categorical data were compared with chi-square analyses whereas continuous data were compared via t-tests with 95% confidence intervals (CIs). Three patient variables, history of allergic reaction, history of asthma, and sex, were placed into a binomial logistic regression model to assess if each variable was an independent predictor of epinephrine administration. We chose these three variables for the model because they have significant associations with one another and there are known sex associations with asthma as well. P-values of <0.05 were used as cut-off values to determine statistical significance. Data were analyzed using the Statistical Package for the Social Sciences, SPSS 19 (SPSS, Inc. Chicago IL). This study received institutional review board approval from Yale University School of Medicine.

Results

Charts for 856 patient visits with ICD-9 codes related to allergic reaction were identified and reviewed. Of these, 638 patient visits were excluded: 613 did not meet criteria for anaphylaxis, 8 patients left without being seen by a provider, 7 were cared for in the adult ED, and 10 were transferred from outside hospitals. Two hundred eighteen cases of anaphylaxis in 202 children were included in the analysis. Twenty-two patients did not meet the diagnostic criteria for anaphylaxis, but had a documented diagnosis of anaphylaxis by the attending physician. Descriptive demographic and medical information as well as symptom presentation and location of onset are provided in Table 2.

Overall, epinephrine was administered to 89 of the 218 (41%) patients prior to PED arrival. **Thirteen patients were given epinephrine by a physician, 18 by a school nurse, 44 by a parent/self, and 14 by an EMS provider.** Patients with a history of allergic reaction were more likely to receive epinephrine prior to PED arrival than those without a prior history (50% vs. 22%, $p < 0.01$). While patients with a history of asthma appeared to received

epinephrine more often than patients without a history of asthma (49% vs. 36%, $p=0.048$), this was no longer significant when sex and allergic history were taken into account through logistic regression. Additionally, there was no significant relationship between allergen types and administration of epinephrine in our sample. Table 3 summarizes the frequency of epinephrine administration among different patient groups.

Ninety patients were transported to the PED by EMS. Of these 90 patients, 44 received epinephrine prior to EMS arrival and 7 did not meet the 2006 anaphylaxis criteria prior to arrival to the ED. Of the remaining 39 patients, EMS administered epinephrine to 14 (36%). Information about the source of administered epinephrine was available for 13 of the 14 patients, all of whom received medication from EMS supplies. Among these 39 patients, 41% received diphenhydramine, 32% received albuterol, and 14% received oxygen. Intravenous fluid therapy was documented in only two patients. Of the 61 patients with full EMS documentation available, the mean time from arrival on scene to arrival in the ED was 28 minutes (SD 10.8, range 3–57). There was no statistically significant difference between time to arrival for those patients receiving epinephrine and those who did not (29.5 vs. 25.5 min, $p=0.17$).

There were 117 patients with a history of known allergies who were with their parents at the time of the anaphylactic reaction. Forty-eight of the 117 (41%) had epinephrine administered by a parent or self-administered the epinephrine, **however only 44 actually received the epinephrine**. Four of these patients did not actually receive their epinephrine due to incorrect use of the autoinjector. There was no significant difference in the use of EMS for transport among this group of 117 patients who did or did not receive epinephrine (39% vs. 33%, $p=0.5$).

Thirteen patients were seen by physicians prior to coming to the PED. All received epinephrine by the physician, but only 10 were sent in by EMS. Two were sent to PED by private car and one patient was sent home by the primary care physician, but presented to the PED with continuing symptoms. Of the 26 patients with anaphylaxis occurring at school, 18/26 (69%) had epinephrine administered by the school nurse. Among the 18 patients that received epinephrine, four had no previous history of allergic reaction. Twenty-two of the 26 school children were brought to the ED by EMS. School nurses had higher rates of epinephrine administration compared to EMS providers and parents ($p=0.016$).

There were no statistically significant differences in epinephrine administration or lack of epinephrine administration in the prehospital setting based on the various organ systems involved or specific allergen type causing the anaphylaxis.

Epinephrine was given to all but three of the remaining 129 patients while in the PED, and 5 patients received second doses of epinephrine. One hundred and forty three of the 218 patient (66%) were discharged home, 70 of the 218 (32%) were admitted to the standard pediatric ward, and 5 of the 218 (2%) went to the pediatric intensive care unit (PICU). There were no deaths related to anaphylaxis.

Of the 89 patients who first received epinephrine in the prehospital setting, 29(33%) were admitted to the hospital and of the 126 patients that received epinephrine in the ED, 46(37%) were admitted to the hospital. There were no significant statistical differences in rates of admission when epinephrine was given in the prehospital settings compared to when epinephrine was given in the ED ($p=0.55$).

Discussion

This study has shown low levels of epinephrine administration during outpatient management of anaphylaxis among children who met the 2006 diagnostic criteria or were diagnosed with anaphylaxis by an attending physician. Our study did not reveal a statistical difference in admission rates between groups when epinephrine was first administered in the prehospital setting.

Early administration of intramuscular epinephrine for anaphylaxis has been associated with improved outcomes such as decreased fatalities, severity of symptoms and biphasic reactions.^{4-9,21} Delayed epinephrine administration, conversely, has been associated with higher rates of biphasic reactions in children.⁶ Among a cohort of patients in the United Kingdom with fatal anaphylactic reactions, the median time to respiratory or cardiac arrest was 30 minutes for foods, 15 minutes for venom, and 5 minutes for iatrogenic reactions.²¹ Notably, epinephrine was administered prior to arrest in only 14% of the patients.²¹

In our study, the rate of epinephrine administration by EMS providers for children meeting criteria for anaphylaxis was only 36%, despite an average transport time of 28 minutes. This is a critical time period where administration of epinephrine, the first line treatment for anaphylaxis, could be life-saving. Additionally, the majority of administered epinephrine was given from EMS' supply. Using patients' own autoinjectors may decrease time to draw up medication, errors in medication dosage and ultimately increase use of epinephrine in the setting of anaphylaxis. The Yale-New Haven Sponsor Hospital Program protocol for pediatric anaphylaxis recommends intravenous fluids, albuterol, and diphenhydramine as first line management of anaphylaxis and only recommends intramuscular epinephrine in the setting of severe cardiopulmonary compromise. This may partially explain the low rates of epinephrine administration by EMS providers, though it is unclear how much the protocol is adhered to, given that only two patients in the cohort transported by EMS received intravenous fluids, which is the first step in the protocol. A recent survey study evaluating knowledge about anaphylaxis in adult patients among paramedics revealed that a very small percentage of paramedics recognized atypical anaphylaxis and less than half of the surveyed paramedics identified epinephrine as the initial drug of choice.²² More education for all EMS providers about the potential severity of anaphylaxis and its first line treatment is necessary and ultimate revision of local EMS protocols may result in increased epinephrine use for pediatric anaphylaxis by EMS providers.

The rate of epinephrine administration by patients or parents, for those with a history of previous allergic reaction was 41% and four parents administered the epinephrine incorrectly. Previous studies have shown similar low treatment rates in this population.^{15,23-27} This is often due to a failure to recognize anaphylaxis, a lack of autoinjector availability, or lack of familiarity with proper techniques for administration.^{18,24,26} Given that anaphylactic reactions occurred at home or with family members 87% of the time, parents and adolescents represent important groups to target when designing educational materials with the goals of improving access to and use of epinephrine autoinjectors, and improving recognition of anaphylaxis and indications for administration of epinephrine.

School nurses in our study had higher rates of epinephrine administration than previously reported, and when compared to EMS providers and parents. Previous studies have shown lower rates of epinephrine administration in school settings due to delayed recognition of anaphylaxis, phone calls to parents, lack of adherence to emergency plans, unsuccessful attempts to administer epinephrine, lack of a physician's order or lack of epinephrine availability at the time of allergic reactions.^{14,26-28} Some of these studies however included

administration of epinephrine by both nurses and staff such as teachers.^{14,26,27} In a recent survey of school nurses in California, where school districts are allowed to stock emergency epinephrine autoinjectors, only 13% reported implementing stock epinephrine programs due to limited availability of school nursing services, inadequate funding for training and medications and lack of education.²⁸ Currently, only 45% of public schools in the U.S. have a full-time nurse on site, while 30% have part time nursing and 25% have no nurses at all. Many states do not permit unlicensed personnel to administer epinephrine to individuals who have not previously received a diagnosis of a life threatening allergy.²⁹ A larger prospective evaluation of epinephrine administration by school nurses may better elucidate the circumstances and the frequency with which epinephrine is administered in the setting of allergic reactions at school.

Finally, our inability to detect a statistical difference in admission rates based on prehospital (or setting of initial) epinephrine administration may have been due to the retrospective nature of our study, which precluded collection of data related to time of initial allergen exposure, onset and progression of symptoms, and total time to epinephrine administration, all of which may be more strongly related to admission rates. Where children receive epinephrine, in the prehospital setting or in the ED, is less important than when they receive it in relation to allergen exposure and progression of symptoms. It is possible that patients with more severe symptoms were more likely to have received epinephrine in the prehospital setting, making interpretation of admission rates difficult. Additionally, while previous studies have reported overall admission rates for pediatric patients with anaphylaxis presenting to the PED from 14.6% to 26.6%, our admission rate was 35%.^{19,20} Variations in practice patterns, such as hospital admission in lieu of prolonged ED observation may contribute to this difference. Finally, although the timing of the epinephrine administration did not affect patient disposition, it is unclear whether this affected ED length of stay or symptom severity on presentation to the ED.

There are several limitations to this study. The retrospective nature of this study precluded the use of standardized ED or EMS documentation of symptoms of anaphylaxis. Reliance on ED medical records limited our ability to discern the true severity of the anaphylactic reaction and the decision-making process by the individual or provider. Additionally, it was not always clear if children with previous allergic reactions had been prescribed an autoinjector, or the severity of previous allergic reactions. EMS charts frequently contained insufficient data to determine with certainty the point at which full anaphylaxis criteria were met prior to PED arrival. As a result, we may have under or over estimated the frequency with which epinephrine was given by various prehospital individuals in the presence of true anaphylaxis.

Conclusions

In our sample of children meeting criteria for anaphylaxis, rates of EMS and parental/self administration of epinephrine in the setting of anaphylaxis were low, despite epinephrine being the first line medication of choice. Additionally, in our study, rates of admission did not differ based on whether epinephrine was given in the prehospital or PED setting. A multicenter prospective evaluation of outpatient management of pediatric anaphylaxis would better characterize the frequency of epinephrine administration by various individuals, symptoms that prompt intervention and barriers to timely administration. It would also allow for more rigorous exploration of the association between timing of medication delivery and relevant patient outcomes such as ED length of stay, rates of hospitalization, illness severity and mortality. Additionally, a more thorough understanding of barriers and facilitators to EMS, parental and school-personnel administration of epinephrine may allow us to better focus educational strategies to improve compliance with this potentially life-saving

treatment. Evaluation and revision of EMS protocols related to pediatric anaphylaxis may also result in improved epinephrine administration by EMS providers in the field.

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Table 1

Anaphylaxis criteria: anaphylaxis is diagnosed when any of the following three criteria are met¹

| |
|---|
| <p>1. Acute onset of illness involving skin, mucosal tissue, or both (hives, pruritis, flushing, swollen lips, tongue, uvula [including subjective symptoms of throat pain, itching, tightness^a]) and at least one of the following:</p> <ul style="list-style-type: none"> A. Respiratory compromise (dyspnea, wheeze, stridor, hoarseness, reduced peak expiratory flow, hypoxemia) B. Reduced blood pressure (BP)^b or associated symptoms of end-organ dysfunction (syncope, incontinence) |
| <p>2. Two or more of the following that occur rapidly after exposure to a likely allergy:</p> <ul style="list-style-type: none"> A. Involvement of the skin–mucosal tissue (described above) B. Respiratory compromise (described above) C. Reduced BP or associated symptoms (described above) D. Persistent gastrointestinal symptoms (crampy abdominal pain, vomiting) |
| <p>3. Reduced BP after exposure to known allergen for that patient</p> |

^aIn 2006, subjective throat symptoms such as throat pain, tightness, and pruritis were reclassified within the skin and mucosal tissue system, not the respiratory system as presented in the 2005 symposium criteria.³

^bLow systolic BP is defined as less than 70 mmHg from 1 month to 1 year of age, less than (70 mmHg + (2 × age in years)) from 1 to 10 years of age and less than 90 mmHg from 11 to 17 years of age, and low diastolic blood pressure is defined as less than 45 mmHg in children greater than 10 years of age.

Table 2

Demographic and descriptive patient information

| Patient characteristics | <i>N</i> = 218 |
|--|------------------------|
| Mean age (SD) | 7.4 years (5.4) |
| Sex, % (<i>n</i>) | |
| Male | 56% ^a (113) |
| Symptoms, % (<i>n</i>) | |
| Skin/mucosal | 98% (214) |
| Respiratory | 68% (149) |
| Gastrointestinal | 44% (96) |
| Hypotension | 2% (5) |
| History of allergic reaction, % (<i>n</i>) | 67% (145) |
| History of asthma, % (<i>n</i>) | 38% (83) |
| Allergens, % (<i>n</i>) | |
| Food products | 76% (165) |
| Medications | 8% (17) |
| Stings | 1% (2) |
| Unknown | 16% (34) |
| Location of initial reaction, % (<i>n</i>) | |
| Home or with family member | 87% (189) |
| School | 12% (26) |
| Physician Office | 1% (2) |
| Other | 0.5% (1) |

^a56% is 113 of the total number of patients, 202, not total patient visits, 218.

Table 3

Prehospital epinephrine administration for patients with anaphylaxis by provider type, allergen, past medical history, and demographics

| | +Epinephrine | -Epinephrine |
|--|------------------------|--------------|
| Females, <i>n</i> = 94 | 50% (47) | 50% (47) |
| Males, <i>n</i> = 124 | 34% (42) | 66% (82) |
| School nurse, <i>n</i> = 26 | 69% (18) | 31% (8) |
| EMS provider, <i>n</i> = 39 | 36% (14) | 64% (25) |
| Parent/self, <i>n</i> = 117 | 41% (48 ^a) | 59% (69) |
| Physician, <i>n</i> = 13 | 100% (13) | 0% (0) |
| Allergen type | | |
| Food, <i>n</i> = 165 | 41% (68) | 59% (97) |
| Drugs, <i>n</i> = 17 | 41% (7) | 59% (10) |
| Bees, <i>n</i> = 2 | 0 | 100% (2) |
| Unknown, <i>n</i> = 34 | 41% (14) | 59% (20) |
| History of allergic reaction, <i>n</i> = 145 | 50% (72) | 50% (73) |
| History of asthma, <i>n</i> = 83 | 49% (41) | 51% (42) |
| Outpatient overall | 40% (87) | 60% (131) |

^aThis calculation includes the 4 patients whose epinephrine was administered incorrectly by parents (44 actual patients received epinephrine by parents/self).