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To cite this article: Eli Carrillo MD, H. Gene Hern MD & Joseph Barger MD (2015): Prehospital Administration of Epinephrine in Pediatric Anaphylaxis, Prehospital Emergency Care, DOI: [10.3109/10903127.2015.1086843](https://doi.org/10.3109/10903127.2015.1086843)

To link to this article: <http://dx.doi.org/10.3109/10903127.2015.1086843>



Published online: 10 Nov 2015.



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PREHOSPITAL ADMINISTRATION OF EPINEPHRINE IN PEDIATRIC ANAPHYLAXIS

Eli Carrillo, MD, H. Gene Hern, MD, Joseph Barger, MD

ABSTRACT

Anaphylaxis in the pediatric population is both serious and potentially lethal. The incidence of allergic and anaphylactic reactions has been increasing and the need for life saving intervention with epinephrine must remain an important part of Emergency Medical Services (EMS) provider training. Our aim was to characterize dosing and timing of epinephrine, diphenhydramine, and albuterol in the pediatric patient with anaphylaxis. In this retrospective chart review, we studied prehospital medication administration in pediatric patients ages 1 month up to 14 years old classified as having a severe allergic reaction or anaphylaxis. We compared rates of epinephrine, diphenhydramine, and albuterol given to patients with allergic conditions including anaphylaxis. In addition, we calculated the rate of epinephrine administration in cases of anaphylaxis and determined what percentage of time the epinephrine was given by EMS or prior to their arrival. Of the pediatric patient contacts, 205 were treated for allergic complaints. Of those with allergic complaints, 98 of 205 (48%; 95% CI 41%, 55%) had symptoms consistent with anaphylaxis and indications for epinephrine. Of these 98, 53 (54%, 95% CI 44%, 64%) were given epinephrine by EMS or prior to EMS arrival. Among the patients in anaphylaxis not given epinephrine prior to EMS arrival, 6 (12%; 95% CI 3%, 21%) received epinephrine from EMS, 10 (20%; 95% CI 9%, 30%) received diphenhydramine only, 9 (18%, 95% CI 7%–28%) received only albuterol and 17 (33%, 95% CI 20%–46%) received both albuterol and diphenhydramine. 9 patients in anaphylaxis received no treatment prior to arriving to the emergency department (18%, 95% CI 7%–28%). In pediatric patients who met criteria for anaphylaxis and the use of epinephrine, only 54% received epinephrine and the overwhelming majority received it prior to EMS arrival. EMS personnel may not be treating anaphylaxis appropriately with epinephrine.

Received September 1, 2014 from Alameda Health System – Highland Hospital, Oakland, California (EC, HGH); Contra Costa County EMS, Martinez, California (JB). Revision received August 6, 2015; accepted for publication August 7, 2015.

Author Contributions: E. Carrillo, H. G. Hern, and J. Barger conceptualized and designed the study; J. Barger carried out initial analysis; and E. Carrillo performed final data analysis. E. Carrillo and J. Barger drafted the initial manuscript. H. G. Hern and E. Carrillo critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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doi: 10.3109/10903127.2015.1086843

PREHOSPITAL EMERGENCY CARE 2015;Early Online:1–6

INTRODUCTION

Anaphylaxis and allergic reactions are serious and potentially lethal diseases in the pediatric population. Although death from anaphylaxis is rare, the incidence of allergic reactions mediated by exposure to foods such as nuts appears to be increasing.^{1–5} Despite the difficulty in determining accurate rates of prevalence and incidence, recent electronic surveys of American household indicate that 8% of children have food allergy and 3% have severe allergies.^{6,7} The primary treatment for anaphylaxis is the administration of epinephrine in a timely fashion.^{8–11} Although it is difficult to determine how many pediatric fatalities are avoided every year through administration of epinephrine in the prehospital setting, it is generally thought that early administration of the drug improves overall mortality.^{12–15}

Although not extensively studied, one case-control study demonstrated that there exists good agreement between Emergency Medical Services (EMS) providers and physicians in recognizing appropriate situations for administration of epinephrine in the prehospital setting.¹⁶ However, the results of more recent studies have called this finding into question. A nationwide survey of paramedics showed that less than half of those who were able to recognize a classic case of anaphylaxis could correctly identify epinephrine as the primary drug of choice.¹⁷ Even when epinephrine was correctly chosen as the drug of choice in simulated pediatric anaphylaxis cases, only half of the providers were able to give the appropriate dose and route.¹⁸ A recent retrospective analysis of prehospital rates of epinephrine administration in an urban tertiary care pediatric ED demonstrated that among children with anaphylaxis, only 36% were given epinephrine by EMS providers prior to their arrival in the emergency department, findings largely consistent with an earlier retrospective study of epinephrine administration in the pediatric population.^{19,20}

Two major reasons are cited for a delay in treatment including 1) correct identification of anaphylaxis and 2) hesitancy to administer epinephrine in pediatric patients who would benefit from early treatment. The criteria for anaphylaxis have undergone numerous revisions, the most recent in 2006, and are now widely accepted (Table 1).²¹ The disparity in those prehospital providers who did not give epinephrine in known

anaphylaxis argues that more efforts are needed to help EMS providers identify this potentially fatal diagnosis. With increasing rates of allergies amongst children, the ability and need for life saving intervention with epinephrine must remain an important part of EMS protocols and provider training.²²

OBJECTIVE

Our study objective was to determine prehospital rates of epinephrine, diphenhydramine, and albuterol administration in pediatric patients who required EMS response for "severe allergies" (as codified on EMS dispatch sheets) or anaphylaxis prior to their transportation to a nearby hospital. Our aim was to determine if pediatric patients were being adequately treated for allergic reactions in the prehospital setting by EMS personnel. Additionally, we were interested in whether personnel other than EMS providers, such as teachers or parents, treated pediatric patients prior to EMS arrival.

METHODS

In this retrospective chart review, we studied medication administration in pediatric patients with allergy or anaphylaxis during our study period of 19 months, from January 1, 2010 to July 10, 2011. We reviewed all charts from the electronic patient care reports for the 19 months in question. We performed a search for pediatric patients and a paramedic initial impression of "Allergy/Anaphylaxis." The records were documented in the electronic software MEDS (Version 2.1.1 for Contra Costa County and V2.2.0A for Alameda County). After filtering for pediatric patients and allergic reaction, we compared rates of epinephrine, diphenhydramine, and albuterol given to patients with allergic conditions (including anaphylaxis). The initial data query searched for patients up to and including 15 years of age. As there were no 15 year olds in our cohort (the mean age of the sample was approximately 5 years old) we analyzed only patients from one month to 14 years of age. The data were independently and blindly reviewed by two investigators (E.C. and J.B.) to determine which cases qualified as anaphylaxis. There was no disagreement between the two investigators that necessitated review from a third investigator. We defined anaphylaxis according to the criteria set forth by the Second Symposium on the Definition and Management of Anaphylaxis Summary Report.²¹

In addition, we calculated the rate of epinephrine administration in cases of anaphylaxis and determined what percentage of time the epinephrine was given by EMS or prior to EMS arrival. Confidence intervals were determined using a Bayesian confidence interval equation for proportions and categorical data were compared using chi-square analyses (GraphPad

TABLE 1. Anaphylaxis criteria

Criteria 1: Acute onset involving skin, mucosal tissue, or both and at least one of the following:
A) Respiratory compromise or B) reduced blood pressure or associated symptoms of end-organ dysfunction (hypotonia, syncope, incontinence)
Criteria 2: After exposure to a likely allergen, two or more of the following:
A) Involvement of the skin/mucosa
B) Respiratory compromise
C) Reduced blood pressure or associated symptoms of end organ damage (syncope, incontinence)
D) Persistent gastrointestinal symptoms (abdominal pain, vomiting)
Criteria 3: Reduced BP after exposure to known allergen
A) Reduced BP in an adult is less than 90 mmHg systolic or 30% decrease compared to baseline systolic BP
B) In infants and children, reduced is low BP by age or 30% decrease in systolic BP

Prism Version 5.0, La Jolla, CA). The use of data in this retrospective study was approved by the Institutional Review Board of the Alameda Health System, Oakland, CA.

RESULTS

Out of 239,320 total patient contacts, 12,898 were pediatric patients (defined as less than 15 years of age) (Figure 1). Of the pediatric patient contacts, 205 were labeled "Allergic Reaction" as the "Primary Impression" by the EMS Prehospital Care Report (PCR). Demographic information, allergen exposure, and location of EMS contact are presented in Table 2. In our sample, allergens with the highest propensity to cause allergic symptoms include tree nuts (27%) as well as peanuts (7%) and fish/seafood products (6%). The majority of offending allergens were not easily determined or documented in the EMS chart, with unknown triggers accounting for 37% of all allergic reactions considered. In patients with allergic complaints, 98 out of 205 (48%; 95% CI 41%–55%) had symptoms consistent with anaphylaxis and indications for epinephrine. Within these 98 who had a clear indication for epinephrine, only 53 children (54%, 95% CI 44%–64%) were given epinephrine. Among those 53 children in whom epinephrine was indicated and given, 47 (89%, 95% CI 80%–97%) were given epinephrine prior to EMS arrival either by parent, school, or a clinic physician. Of the 51 patients who might have benefited from epinephrine from EMS, 6 (12%, 95% CI 3%–21%) received epinephrine, 10 (20%, 95% CI 9%–30%) received only diphenhydramine, 9 (18%, 95% CI 7%–28%) received only albuterol and 17 (33%, 95% CI 20%–46%) received both albuterol and diphenhydramine. 9 patients in anaphylaxis received no treatment prior to arriving to the emergency department (18%, 95% CI 7%–28%).

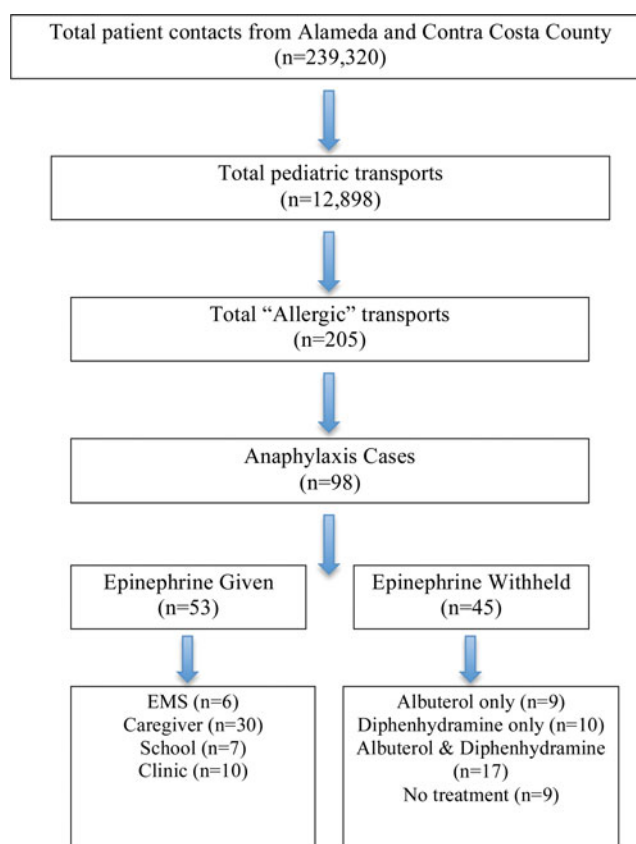


FIGURE 1. Patient identification flowchart.

There was no statistical difference between the rates of anaphylaxis between the two counties surveyed ($p = 0.3871$) nor was there a difference based on sex ($p = 1.0$) (Table 3). There were a total of 77 patients who had a history of a prior allergic reaction per parental report and who also qualified as meeting anaphylaxis criteria. Of those patients, only 46 (60%) received epinephrine and 7 (9%) received no treatment at all. Patients with anaphy-

laxis and a history of an allergic reaction were much more likely to receive epinephrine compared to those without an allergic history (48% vs. 5%, $p < .0053$) (Table 4). One patient was given epinephrine by EMS despite having no clear signs of anaphylaxis, as was one patient who presented to their primary care doctor. For patients with a prior history of an allergic reaction or anaphylaxis, 52% of parents were able to administer epinephrine prior to EMS arrival. Of note, one parent accidentally injected herself with the child's epinephrine auto-injector while trying to administer the medication. Of patients who received epinephrine prior to the arrival of EMS, 21% of patients received their epinephrine from a primary care provider and 79% from parents/caregivers or school personnel. All 6 of the patients who suffered from an anaphylactic reaction in a school setting were given epinephrine whereas 10 out of 11 patients who presented to a pediatric or primary care clinic with anaphylaxis were given the appropriate treatment. It was unclear from the charts if the patients at school received their own epinephrine injections or if they used the school's supply of epinephrine.

Overall, diphenhydramine was the preferred medication administered by EMS. A total of 41% of all patients received diphenhydramine, whereas 20% received albuterol, regardless of whether they were

TABLE 2. Demographics

N = 205		
Mean Age in years (SD)	5.25 (4)	
Sex, Male% (n)	59% (121)	
Allergens,% (n)		
	Unknown	37% (75)
	Nuts	27% (55)
	Other Food	11% (22)
	Peanuts	7% (15)
	Fish/Shellfish	6% (12)
	Egg	4% (8)
	Milk	2% (5)
Location of EMS contact,% (n)		
	Home	90% (185)
	School	5% (10)
	Clinic	5% (10)

TABLE 3. Anaphylaxis rate

Total Cases	Allergic Cases% (N)	Anaphylaxis% (N)	Anaphylaxis% (95% CI)
Alameda County	67 (137)	67 (66)	
Contra Costa County	33 (68)	33 (32)	
Total (N)	205	98	48 (41–55)

having an allergic reaction or anaphylaxis. Among cases where EMS providers should have administered epinephrine, they gave both albuterol and diphenhydramine in combination 33% of the time (95% CI, 20%–46%).

DISCUSSION

Of the 12,898 pediatric EMS contacts made during the time period, 1.5% were made for “Allergic Reactions” and only 0.76% were deemed to be true cases of anaphylaxis. Although it is difficult to obtain accurate data on the prevalence of pediatric anaphylaxis due to varying definitions and heterogeneity of studies, our percentage of EMS contact with anaphylaxis in pediatric patients appears to be consistent with previously described rates of 0.4% to 0.9%.^{5,23} The most concerning finding is that in instances where EMS personnel were in a position to administer the appropriate treatment for anaphylaxis, they did so only 12% of the time, instead preferring to administer albuterol and/or diphenhydramine. Even more concerning, 7 patients in anaphylaxis who had a documented history of allergic reactions received no treatment whatsoever.

It is unclear from the electronic medical records why epinephrine was withheld in cases of anaphylaxis. Most of the documentation done by EMS providers indicates that anaphylaxis was either not considered or that the patient was more likely seen as merely “allergic” thereby necessitating other symptomatic treatments. Schools were most successful in administering the epinephrine to all of their students with anaphy-

laxis. It is expected that this success will continue now that California law requires public schools to provide epinephrine auto-injectors to school nurses or trained volunteers.²⁴ Parents or caregivers were successful in giving epinephrine to patients with known allergic reactions or anaphylaxis about 52% of the time. We are unable to determine if approximately half of the parents who did not give epinephrine did so because they did not have an epinephrine pen or because they felt unprepared to administer the drug. We know from prior studies that caregivers are often feel unprepared and untrained when administering an intramuscular injection.²⁵ Given that these children had documented allergic reactions in the past, it indicates that more of an onus must also be placed on primary care and emergency department physicians in recognizing the high-risk nature of these reactions and their propensity to recur. We would argue that the benefits of prescribing multiple epinephrine pens and engaging in high quality teaching regarding the risk of anaphylaxis appear to outweigh any risks of inappropriate administration or the burden of medication cost.

Overall, the difficulty in detecting anaphylaxis is partially due to the very low incidence of the disease in the pediatric population, unfamiliarity with pediatric patients, unease with the administration of epinephrine for non-cardiac arrest indications, and clinical criteria which have not yet been fully disseminated and incorporated into EMS provider training.

The data in this study suggest that our EMS system is currently not recognizing and not properly administering potentially life-saving medications. Possible interventions to improve EMS recognition include continued education about the clinical signs of anaphylaxis, review of pediatric specific case studies, and the use of a portable, handheld, easy to understand guidelines for use in the initial prehospital encounter. More education and practice with using the epinephrine pen injector is required for both caregivers and school personnel.

Finally, our data are consistent with a prior study showing less than half of patients meeting criteria were given epinephrine.¹⁷ That study was done at a single urban tertiary hospital receiving center. Our study is markedly different in that it covers two distinct geographic areas with multiple types of receiving hospitals (urban, suburban, teaching, HMO) and represents a dispatch area encompassing over 1455 square miles and 2.5 million people. Together, both studies reinforce the notion that anaphylaxis is likely being undertreated by EMS personnel, regardless of the setting.

LIMITATIONS

The results of this study are limited in that this is a retrospective study based on chart review of electronic medical records submitted by EMS providers.

TABLE 4. Allergy history and anaphylaxis

	Total = N
Known allergy received epinephrine (all sources)	46
Known allergy received albuterol and/or diphenhydramine	23
Known allergy received nothing	7
Without allergy received epinephrine (all sources)	7
Without allergy received albuterol and/or diphenhydramine	15
Without allergy received nothing	0
	N = 98

We did not obtain hospital records to determine if those patients who met anaphylaxis criteria in the prehospital setting were eventually treated with epinephrine by emergency department physicians. We are also unable to obtain the patients' overall clinical course and whether the delay to receiving epinephrine caused any detrimental outcome. Additionally, patients who received epinephrine prior to EMS arrival were included in the statistical count for patients requiring epinephrine. Given the nature of retrospective chart reviews and the concise format of EMS charts, it was often difficult to determine the progression of symptoms and the time that anaphylaxis criteria were met. It is not possible to determine if clinical improvement after administration of other medications, in lieu of epinephrine, caused providers to forgo epinephrine treatment entirely.

There are many possible reasons why epinephrine was not administered. It may be that the EMS personnel thought the case was only a mild allergic reaction and weren't aware of the anaphylaxis criteria. First responders may have felt that there was some diagnostic uncertainty or that an ultra short transport time might have mitigated the need for epinephrine. Most of the major national and international allergy and anaphylaxis guidelines, however, call for early administration of epinephrine if the criteria are met. Based on our chart reviewers, the criterion were met and the lack of epinephrine administration would be considered failing to adhere to protocol. It is possible that parent or patient refusal could have played a role or that developing criteria late in the transport might have led to fewer administrations. Those reasons for delay were not outlined in the chart. Lastly, although protocols at the time of the patient encounter clearly delineate the proper medications to administer in anaphylaxis, it is important to note that the National Association of EMS Physicians Position Statement on the use of epinephrine in out-of-hospital anaphylaxis was published in the last few months of this study's timeframe.²² It is unclear if rates of epinephrine administration have improved after allowing for the dissemination of the position paper throughout the EMS systems in these two counties.

CONCLUSIONS

In anaphylaxis patients who met criteria for epinephrine, only 52% received epinephrine and the overwhelming majority received it prior to EMS arrival. In our EMS systems, providers were far more likely to give diphenhydramine or albuterol than epinephrine in patients who met criteria for epinephrine.

Unfortunately, EMS personnel are not treating anaphylaxis appropriately or consistently with epinephrine. In addition, children with anaphylactic

complaints are far more likely to receive appropriate therapy prior to EMS arrival, further reinforcing the current practice that parents and other caregivers (including schools) should continue to be educated on the recognition and treatment of allergic reactions including anaphylaxis.

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