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Management of anaphylaxis after pre-hospital epinephrine use in children with food-induced anaphylaxis

Lauren Perlman, MDCM(c)[*]; Sofianne Gabrielli, MSc[*]; Ann E. Clarke, MD, MSc[†]; Luca Delli Colli, MSc[*]; Marina Delli Colli, BScN[*]; Judy Morris, MD, MSc[‡]; Jocelyn Gravel, MD, MSc[§]; Rodrick Lim, MD[‖]; Edmond S. Chan, MD[¶]; Ran D. Goldman, MD[#]; Andrew O'Keefe, MD, MPH[**]; Jennifer Gerdts, BComm[††]; Derek K. Chu, MD, PhD[‡‡]; Julia Upton, MD, MPH[§§]; Elana Hochstadter, MD[‖‖]; Jocelyn Moisan, MD, MSc[¶¶]; Adam Bretholz, MD[##]; Christine McCusker, MD, MSc[*]; Xun Zhang, PhD[***]; Jennifer L.P. Protudjer, PhD[†††,‡‡‡]; Elissa M. Abrams, MD, MPH[†††]; Elinor Simons, MD, PhD[†††]; Moshe Ben-Shoshan, MD, MSc[*]

[*] *Division of Pediatric Allergy, Clinical Immunology, and Dermatology, Montreal Children's Hospital, McGill University Health Centre, Montreal, Quebec, Canada*
[†] *Division of Rheumatology, Department of Medicine, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada*
[‡] *Department of Emergency Medicine, Hôpital Sacré-Coeur, Montreal, Quebec, Canada*
[§] *Department of Pediatric Emergency Medicine, Centre Hospitalier Universitaire Sainte-Justine, Université de Montréal, Montreal, Quebec, Canada*
[‖] *Division of Pediatric Emergency Medicine, Department of Pediatrics, Schulich School of Medicine and Dentistry, University of Western Ontario, London, Ontario, Canada*
[¶] *Division of Allergy, Department of Pediatrics, BC Children's Hospital, University of British Columbia, Vancouver, British Columbia, Canada*
[#] *Division of Clinical Pharmacology and Emergency Medicine, Department of Pediatrics, BC Children's Hospital, University of British Columbia and the BC Children's Research Institute, Vancouver, British Columbia, Canada*
[**] *Department of Pediatrics, Faculty of Medicine, Memorial University, St. John's, Newfoundland, and Labrador, Canada*
[††] *Food Allergy Canada, Toronto, Ontario, Canada*
[‡‡] *Division of Clinical Immunology and Allergy, Department of Medicine and Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, Ontario, Canada*
[§§] *Division of Immunology and Allergy, Department of Pediatrics, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada*
[‖‖] *Department of Pediatric Emergency Medicine, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada*
[¶¶] *Emergency Medical Services of Outaouais, Outaouais, Quebec, Canada*
[##] *Division of Pediatric Emergency Medicine, Department of Pediatrics, Montreal Children's Hospital, Montreal, Quebec, Canada*
[***] *Centre for Outcomes Research and Evaluation, Research Institute of McGill University Health Centre, Montreal, Quebec, Canada*
[†††] *Department of Pediatrics and Child Health, Rady Faculty of Health Sciences, University of Manitoba and Children's Hospital Research Institute of Manitoba, Winnipeg, Manitoba, Canada*
[‡‡‡] *Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden*

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ABSTRACT

Background: Previous guidelines recommend prompt epinephrine administration, followed by observation in the emergency department (ED). The need for transfer in all cases of anaphylaxis has recently been challenged.
Objective: To evaluate the need for additional ED treatment among children with anaphylaxis who received pre-hospital epinephrine.
Methods: Between 2011 and 2023, data were collected on symptoms, triggers, comorbidities, and prehospital and in-hospital management from children (<18 years) with food-induced anaphylaxis who received at least 1 dose of prehospital epinephrine presenting at 7 pediatric EDs. Multivariable logistic regression assessed factors associated with the use of 2 or more prehospital epinephrine autoinjectors (EAIs), epinephrine use in the ED, and hospital admission.
Results: Of the 1127 children (mean 8.1 ± 5.3 years; 60.6% male sex) with food-induced anaphylaxis who used at least 1 EAI prehospital, the most common trigger was peanuts (25.3%). There were 209 (18.5%) children who received additional epinephrine in the ED, most of whom (88.0%) received 1 dose. A total of 30 (2.7%) patients were admitted to hospital. Among all patients, severe reactions (cardiovascular instability/cyanosis/loss of consciousness) (adjusted odds ratio [aOR] 1.22; 95% CI 1.12-1.33) and reactions to tree nuts (aOR 1.09; 95% CI 1.03-1.16) were associated with increased odds of in-hospital epinephrine use. Prehospital inhaled β-agonists

Address correspondence to: Lauren Perlman, MDCM(c), Division of Pediatric Allergy, Clinical Immunology and Dermatology, 1001 Decarie Blvd, Montreal, QC H4A 3J1, Canada
E-mail: lauren.perlman@mail.mcgill.ca.

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(aOR 1.08; 95% CI 1.01-1.16) use and severe reactions (aOR 1.13; 95% CI 1.05-1.22) were associated with the use of 2 or more EAI prehospital.

Conclusion: A minority of anaphylaxis cases that used prehospital EAIs required additional treatment, supporting that shared decision making about transfer to ED works for most patients.

Introduction

Prompt epinephrine administration is the first-line treatment for anaphylaxis. Nevertheless, epinephrine autoinjectors (EAIs) are suboptimally used, with only 20.0% of children receiving epinephrine in the prehospital setting.[1] Patients diagnosed with anaphylaxis are recommended to carry 2 EAIs with them at all times. Previous practice parameters for anaphylaxis recommend prompt epinephrine administration, followed by observation in the emergency department (ED) until symptoms have resolved.[2] However, data now emphasizes shared decision making regarding transfer in all cases of anaphylaxis after epinephrine, with a strong focus on counseling patients and families on when to promptly activate emergency medical services (EMS).[3-5] The 2023 anaphylaxis parameter states that "immediate activation of EMS may not be required if the patient experiences prompt, complete, and durable response to treatment with epinephrine, provided that additional epinephrine and medical care are readily available if needed. [It is suggested] that clinicians counsel patients to always activate EMS after epinephrine use if anaphylaxis is severe, fails to resolve promptly, fails to resolve completely or nearly completely, or returns, or worsens after a first dose of epinephrine."[3] Therefore we aimed to assess the risk factors and demographics of children who required additional management among those known for anaphylaxis who received 1, 2, or 3 or more EAI prehospital.

We suggest that clinicians counsel patients that immediate activation of EMS may not be required if the patient experiences a prompt, complete, and durable response to treatment with epinephrine, provided that additional epinephrine and medical care are readily available if needed. We suggest that clinicians counsel patients to always activate EMS after epinephrine use if anaphylaxis is severe, fails to resolve promptly, fails to resolve completely or nearly completely, or returns, or worsens after a first dose of epinephrine.

Methods

Study Design

In this observational cross-sectional study, children younger than 18 years old who presented with anaphylaxis were recruited from 7 participating hospitals to the Cross-Canada Anaphylaxis REgistry (C-CARE). From April 15, 2011 to September 25, 2023, data were collected both prospectively and retrospectively. Prospective standardized C-CARE data involved the collection of data from parents/legal guardians whose children presented to the ED and who had provided informed consent. Retrospective data were collected through a structured chart review on the basis of the International Classification of Diseases (10th revision) codes for anaphylaxis (described under the "Outcomes and Independent Variables" section.[6]

Participants included in the current study were children known for food-induced anaphylaxis, presenting to EDs with anaphylaxis after at least 1 dose of prehospital EAI. The suspected allergen was determined and reported on the basis of patient and parental reports and the physician's judgment. Reactions to nuts within the registry only included patients who consumed peanuts and tree nuts simultaneously, making families or physicians unable to decipher which allergen caused the reaction. If patients consumed either peanuts or tree nuts independently, those respective triggers were documented as separate variables, rather than in the "nuts" category. Participants were excluded if the case did not meet the National Institute of Allergy and Infectious Diseases definition of anaphylaxis, as reviewed independently by 2 research team members (M.B.S. and L.P.).[7]

Setting

The study included 7 EDs in 4 Canadian provinces (British Columbia, Ontario, Quebec, and Newfoundland and Labrador). In Quebec, participants were recruited from the following 3 centers: the Montreal Children's Hospital, Hôpital Sainte-Justine, and Hôpital du Sacré-Coeur. The other 4 EDs included in the C-CARE data set for this study were British Columbia Children's Hospital, The Hospital for Sick Children (SickKids) and London Health Sciences Center in Ontario (Western), and Janeway Children's Health and Rehabilitation Centre (Janeway) in Newfoundland and Labrador.

Outcomes and Independent Variables

The primary outcomes of interest were participants who received 2 or more prehospital EAI, patients who received epinephrine in the ED, and who required hospital admission. Patients who received 2 prehospital EAIs were assessed separately as guidelines suggest carrying 2 EAIs at all times. Independent variables assessed in this study included demographics (age and sex), culprit food, clinical characteristics of the reaction (symptoms and severity), comorbidities (known eczema and asthma), and treatment (inpatient and outpatient).

Using the symptoms reported in C-CARE, a modified grading system classified the severity of anaphylaxis as mild, moderate, or severe.[8,9] The reaction was classified by its most severe symptom. Mild reactions involved generalized pruritus, urticaria, angioedema, flushing, nausea, or vomiting, mild abdominal pain, nasal congestion, and/or sneezing, rhinorrhea, throat tightness, mild wheezing, tachycardia, and anxiety. Moderate reactions were defined as crampy abdominal pain, diarrhea, recurrent vomiting, "barky" cough, hoarseness, difficulty swallowing, dyspnea, moderate wheezing, and lightheadedness. Severe reactions involved cyanosis, respiratory arrest, hypotension, and/or circulatory collapse, dysrhythmia, loss of bowel control, severe bradycardia, and/or cardiac arrest, confusion, and loss of consciousness.[8]

Statistical Analysis

The participants' demographics and clinical characteristics were summarized as median (IQR) for continuous data (age) and as proportions for categorical data. Proportion testing was performed to assess for differences in the above variables between patients who received 1 prehospital EAI (our reference group), vs 2 or 3 or more prehospital EAI use. All variables other than age were dichotomized. Univariable and multivariable logistic regressions were performed to assess factors associated with multiple prehospital EAI, admission, and additional epinephrine in the ED, adjusted for age and sex, reaction severity, comorbidities, and additional prehospital management. The significance level was set at 0.05. All statistical analyses were performed using R version 4.2.0 (R Core Team 2013; R Foundation for Statistical Computing, Vienna, Austria).

Ethics Approval

Each site's Ethics Committee approved this study. Informed consent was obtained for all participants recruited prospectively.

Results

Demographics, Prevalence, and Clinical Characteristics

From April 2011 to September 2023, a total of 1127 children with known food-induced anaphylaxis who received prehospital epinephrine were enrolled in C-CARE, comprising 19.6% (n = 5737) of the registry. In the present study, 77.9% of participants were recruited from Quebec (n = 878), and 65.0% of cases were recruited retrospectively (n = 732) (Table 1). The median age at reaction was 7.0 (IQR 9.8), and 683 (60.6%) were of the male sex. Mucocutaneous symptoms, notably pruritus (533; 47.3%), urticaria (624; 55.4%), and angioedema (585; 51.9%) were the most common. More than a third experienced respiratory symptoms; 445 (39.5%) experienced throat tightness and 454 (40.3%) had breathing difficulties. There were 415 (36.8%) patients who had gastrointestinal symptoms. A total of 89 (7.9%) reactions were severe. Cardiovascular symptoms were rare; 21 had cyanosis (1.9%), 5 (0.4%) had circulatory collapse, and 27 (2.4%) had hypotension.

The main triggers of anaphylaxis were peanuts (285; 25.3%) and tree nuts (177; 15.7%), which were also among the most common food allergies, at 49.4% and 23.2%, respectively. Asthma and eczema were reported in 197 (17.5%) and 145 (12.9%) participants, respectively. More than half of the study participants' reactions occurred at home (591; 52.4%). All reactions occurred by means of ingestion of the allergen.

All patients in the study received at least 1 dose of epinephrine before presentation to the hospital for evaluation. Most (950; 84.3%) received only 1 dose prehospital, 140 received 2 doses prehospital (12.4%), whereas a few received 3 or more doses (37; 3.3%). Nearly half of the participants received antihistamines as an outpatient (507; 45.0%), whereas 118 received β-agonists (10.5%). A minority (16; 1.4%) received corticosteroids prehospital.

In the ED, 209 study participants (18.5%) received additional intramuscular epinephrine. Nearly all (184/209; 88.0%) received 1 dose, whereas few received 2, 3, or more (n = 20 and n = 5, respectively). There were 10 patients (0.9%) who required intravenous epinephrine, 417 (37.0%) received antihistamines, 89 (7.9%) had β-agonist therapy, and 38 received intravenous fluids. Nearly one-quarter of patients (294; 26.1%) received corticosteroids.

In total, 70 patients (6.2%) required 3 or more doses of epinephrine as treatment for their anaphylaxis (combined prehospital and in-hospital). This is likely because of strict anaphylaxis definitions. A total of 50% of patients with severe reactions received additional epinephrine (n = 45). There were 2.7% who required admission: 17 (1.5%) required admission to the wards and 13 (1.2%) required intensive care unit admission.

Differences Between Proportions Between Patients Who Received 1 Prehospital Epinephrine Autoinjector vs 2, 3, or More Prehospital Epinephrine Autoinjector

Patients who received 2, or 3 or more EAIs prehospital were significantly more likely to have severe reactions compared with the reference group, who received 1 prehospital EAI (2 vs 1: difference 4.6, 95% CI 1.3-10.5; 3 or more vs 1: difference 14.8, 95% CI 0.1-29.5).

Interestingly, patients who received 2 EAI were significantly more likely to have reactions to peanuts than our reference group (difference 5.7, 95% CI 1.1-18.6). However, those who received 1 EAI were much more likely to have a reaction to egg than those who received 3 or more (difference 7.7, 95% CI 4.6-10.8).

Patients who had 3 or more prehospital EAIs were more likely to receive intravenous epinephrine in the ED (difference 13.2, 95% CI 0.8-25.6), and corticosteroids (difference 18.8, 95% CI 1.2-36.4), and intravenous fluids (difference 16.6, 95% CI 2.5-30.6).

Significantly more patients who received 2 prehospital EAIs vs 1 dose received inhaled β-agonists (difference 5.2, 95% CI 0.9-11.3), and corticosteroids (difference 8.5, 95% CI 0.2-17.1), in the ED.

Patients who received only 1 prehospital EAI were significantly less likely to be admitted than those who received 2 (difference −5.2, 95% CI −10.2 to −0.2) or 3 or more prehospital EAIs (difference −19.0, 95% CI −33.7 to −4.4).

Factors Associated With 2 or More Doses of Epinephrine Prehospital

Severe reactions (adjusted odds ratio [aOR] 1.13; 95% CI 1.05-1.22), use of β-agonists prehospital (aOR 1.08; 95% CI 1.01-1.16), and increasing age (aOR 1.01; 95% CI 1.00-1.01) were associated with requiring 2 or more EAIs before presentation to the ED when also adjusted for sex (Table 2).

Factors Associated With an Additional Dose of Epinephrine in Hospital Among All Patients

Severe reactions (aOR 1.22; 95% CI 1.12-1.33) and reactions to tree nuts (aOR 1.09; 95% CI 1.03-1.16) were associated with increased odds of an additional dose of epinephrine in a hospital when adjusted for age and male sex (Table 3).

Factors Associated With Admission Among All Patients

Severe reactions were associated with hospital admission (whether wards or intensive care unit) among all patients (aOR 1.09, 95% CI 1.05-1.12) requiring prehospital EAI when adjusted for age and male sex (Table 4).

Discussion

To our knowledge, we conducted the largest Canadian study to assess the need for additional medical care after prehospital EAI use for food-induced anaphylaxis in children. Our results revealed that only a minority of patients who used EAI required additional ED treatment including epinephrine. Reactions to tree nuts were more likely to require additional epinephrine in the hospital, along with severe reactions. Patients who received inhaled β-agonists prehospital were more likely to receive 2 or more EAI prehospital. Those with severe reactions are more likely to be hospitalized.

Tree nut anaphylaxis accounts for 18% to 40% of anaphylaxis cases, with 70% to 90% of anaphylaxis fatalities being due to peanuts and tree nuts.[10] Accidental ingestion of tree nuts is very common, with 66% of individuals in 1 study having more than 5 reactions in their lifetime.[11] Specifically, cashew and pistachio allergies are known to cause severe reactions with exposure to a small quantity of allergen and it was recently reported that cashew vs peanut may be associated with more persistent and severe allergy.[10] Furthermore, studies by our group suggest that the rate of tree nut-induced anaphylaxis is increasing.[7] Overall, our study results align with various other studies, which suggest that prolonged observation should be encouraged in anaphylaxis with severe reactions caused by peanuts/tree nuts.[12] In addition, there is seemed to be an increased risk of biphasic reactions, and severe or fatal food-induced anaphylaxis in patients with tree nut allergies and those with asthma.[13] Education should, therefore, be emphasized in these patients, who, as aforementioned, have a higher risk for recurrence of anaphylaxis and severe reactions.[14]

Asthma and anaphylaxis are both atopic conditions that frequently coexist, linked by mast cells. Almost 20% of patients in our

Table 1
Demographics, Clinical Characteristics, and Treatments of Participating Children Who Received Prehospital Epinephrine

Variables	Participating children, n (%)					
	1 dose of prehospital epinephrine n = 950	2 doses of prehospital epinephrine n = 140	3+ doses of prehospital epinephrine n = 37	Total N = 1127	Difference%, 95% CI (1 vs 2)	Difference%, 95% CI (1 vs 3+)
Province:						
British Columbia	90 (9.5)	7 (5.0)	0 (0.0)	97 (8.6)	4.5 (0.0-8.9)[a]	9.5 (6.2-12.7)[a]
Newfoundland and Labrador	5 (0.5)	2 (1.4)	0 (0.0)	7 (0.6)	−0.9 (−3.3 to 1.4)	0.5 (−0.4 to 1.5)
Ontario	130 (10.6)	14 (10.0)	1 (2.7)	145 (12.8)	3.7 (−2.2 to 9.5)	11.7 (3.9-18.0)[a]
Quebec	725 (76.3)	117 (83.6)	36 (97.3)	878 (77.9)	−7.3 (−14.4 to −0.1)[a]	−21.0 (−28.3 to −13.7)[a]
Age at reaction (y), median (IQR)	6.8 (3.0-12.4)	9.2 (4.0-14.4)	13.3 (5.7-15.3)	7.0 (3.2-13.0)	NA	NA
Age at reaction (y), mean (SD)	7.8 (5.2)	9.2 (5.4)	10.7 (5.4)	8.1 (5.3)	NA	NA
Sex, male	583 (61.4)	81 (57.9)	19 (51.4)	683 (60.6)	3.5 (−5.6 to 12.7)	10.4 (−7.8 to 27.8)
Sex, female	367 (38.6)	59 (42.1)	18 (48.6)	444 (39.4)	−3.5 (−12.7 to 5.6)	10.0 (−27.8 to 7.9)
Reaction severity:						
Mild	156 (16.4)	15 (10.7)	2 (5.6)	173 (15.4)	5.7 (0.3-11.8)[a]	11.0 (1.9-20.1)[a]
Moderate	729 (76.7)	109 (77.9)	27 (73.0)	865 (76.8)	−1.1 (−8.9 to 6.7)	3.7 (−12.2 to 19.7)
Severe	65 (6.8)	16 (11.4)	8 (21.6)	89 (7.9)	−4.6 (−10.5 to −1.3)[a]	−14.8 (−29.5 to −0.1)[a]
Primary triggers:						
Peanut	232 (24.4)	48 (34.3)	5 (13.5)	280 (25.3)	−5.7 (−18.6 to −1.1)[a]	10.9 (−1.8 to 23.7)
Tree nut	150 (15.8)	18 (12.9)	9 (24.3)	177 (15.7)	2.9 (−3.5 to 9.4)	−8.5 (−24.0 to 6.9)
Nut	88 (9.3)	17 (12.1)	4 (10.8)	109 (9.7)	−2.9 (−9.0 to 3.2)	−1.6 (−13.1 to 10.0)
Milk	100 (10.5)	18 (12.9)	7 (18.9)	125 (11.1)	−2.3 (−8.6 to 3.6)	−8.4 (−22.6 to 5.8)
Egg	73 (7.7)	6 (4.3)	0 (0.0)	79 (7.0)	3.4 (−0.8 to 7.6)	7.7 (4.6 to 10.8)[a]
Prehospital treatments:						
Intramuscular epinephrine	950 (100.0)	140 (100.0)	37 (100.0)	1 dose: 950 (84.3) 2 doses: 140 (12.4) 3 doses: 22 (1.9) 4 doses: 12 (1.1) 5 doses: 2 (0.2) 6 doses: 1 (0.1)	0 (0-0)	0 (0-0)
Antihistamines	437 (46.0)	57 (40.7)	13 (35.1)	507 (45.0)	5.3 (−3.9 to 14.4)	10.9 (−6.2 to 28.0)
Anti-H_2	9 (0.9)	1 (0.7)	0 (0.0)	10 (0.9)	0.2 (−1.5 to 2.0)	0.9 (−0.6 to 2.5)
β-agonists	90 (9.5)	21 (15.0)	7 (18.9)	118 (10.5)	−5.5 (−12.1 to 10.8)	−9.4 (−23.6 to 4.7)
Corticosteroids	13 (1.4)	1 (0.7)	2 (5.4)	16 (1.4)	−0.7 (−1.3 to 2.6)	−4.0 (−12.8 to 4.7)
Intravenous fluids	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0-0)	0 (0-0)
No treatment	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0.2 (−0.3 to 0.7)	0.2 (−0.3 to 0.7)
In-hospital treatments:						
Additional intramuscular epinephrine	180 (18.9)	19 (13.6)	10 (27.0)	209 (18.5)	5.3 (−1.2 to 12.0)	−8.1 (−24 to 7.8)
Additional intramuscular epinephrine, mean (SD)	1.11 (0.4)	1.37 (0.5)	1.30 (0.5)	1.15 (0.5)	NA	NA
1 dose	165 (17.4)	12 (8.6)	7 (18.9)	184 (16.3)	12.4 (7.6-17.2)[a]	−1.5 (−15.8 to 12.7)
2 doses	10 (1.1)	7 (5.0)	3 (8.1)	20 (1.8)	−4.6 (−8.0 to 0.0)	−7.1 (−17.3 to 3.2)
3+ doses	5 (0.5)	0 (0.0)	0 (0.0)	5 (0.4)	0.5 (−0.3 to 1.4)	0.5 (−0.5 to 1.5)
Intravenous epinephrine	3 (0.3)	2 (1.4)	5 (13.5)	10 (0.9)	−1.1 (−3.5 to 1.3)	−13.2 (−25.6 to −0.8)[a]
Antihistamines	342 (36.0)	61 (43.6)	14 (37.8)	417 (37.0)	−7.6 (−16.7 to 1.6)	−1.8 (−19.2 to 15.5)
Anti-H_2	65 (6.8)	15 (10.7)	5 (13.5)	85 (7.5)	−3.9 (−9.7 to 19.1)	−6.7 (−19.2 to 5.9)
β agonists	66 (6.9)	17 (12.1)	6 (16.2)	89 (7.9)	−5.2 (−11.3 to −0.9)[a]	−9.3 (−22.7 to 4.1)
Corticosteroids	232 (24.4)	46 (32.9)	16 (43.2)	294 (26.1)	−8.5 (−17.1 to −0.2)[a]	−18.8 (−36.4 to −1.2)[a]
Intravenous fluids	22 (2.5)	9 (6.4)	7 (18.9)	38 (3.4)	−4.1 (−8.7 to 0.4)	−16.6 (−30.6 to −2.5)[a]
No treatment	48 (5.1)	6 (3.4)	0 (0.0)	54 (4.8)	0.8 (−3.2 to 4.8)	5.1 (2.3-7.8)[a]

(*continued*)

Table 1 (*Continued*)

Variables	Participating children, n (%)					
	1 dose of prehospital epinephrine n = 950	2 doses of prehospital epinephrine n = 140	3+ doses of prehospital epinephrine n = 37	Total N = 1127	Difference%, 95% CI (1 vs 2)	Difference%, 95% CI (1 vs 3+)
Known atopic conditions						
Known food allergy	950 (100.0)	140 (100.0)	37 (100.0)	1127 (100.0)	0 (0-0)	0 (0-0)
Peanut	466 (49.1)	75 (53.6)	16 (43.2)	557 (49.4)	−4.5 (−13.8 to 4.7)	5.8 (−11.9 to 23.5)
Tree nut	226 (23.8)	26 (18.6)	9 (24.3)	261 (23.2)	5.2 (−2.2 to 12.6)	−0.5 (−15.2 to 14.1)
Nut	198 (20.8)	27 (19.3)	7 (18.9)	232 (21.4)	1.5 (−5.9 to 9.0)	1.9 (−12.4 to 16.2)
Milk	175 (18.4)	25 (17.9)	10 (27.0)	210 (18.6)	−0.6 (−6.7 to 7.8)	−8.6 (−24.5 to 7.3)
Egg	238 (25.1)	26 (18.6)	7 (18.9)	271 (24.0)	6.5 (−0.9 to 13.9)	6.1 (−8.2 to 20.4)
Sesame	105 (11.1)	7 (5.0)	4 (10.8)	116 (10.3)	6.0 (1.5-10.6)[a]	0.2 (−10.2 to 10.7)
Known asthma	163 (17.2)	28 (20.0)	6 (16.2)	197 (17.5)	−2.8 (−10.3 to 4.6)	0.9 (−12.1 to 14.0)
Known eczema	128 (13.5)	14 (10.0)	3 (8.1)	145 (12.9)	3.5 (−2.4 to 9.4)	5.4 (−5.1 to 15.8)
Regular treatments:						
β-blockers	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.2)	0.2 (−0.3 to 0.7)	0.2 (−0.3 to 0.7)
MAOi	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0-0)	0 (0-0)
Tricyclic antidepressants	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0.1 (−0.2 to 0.4)	0.1 (−0.2 to 0.4)
ACE inhibitors	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.1)	−0.7 (−2.5 to 1.1)	0 (0-0)
NSAIDs	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0.1 (−0.2 to 0.4)	0.1 (−0.2 to 0.4)
Admission status:						
Not admitted	925 (97.4)	129 (92.1)	29 (78.4)	1083 (96.1)	5.2 (0.2-10.2)[a]	19.0 (4.3-33.7)[a]
Admit to hospital wards	8 (0.8)	6 (4.3)	3 (8.1)	17 (1.5)	−3.4 (−7.3 to −0.4)[a]	−7.3 (−17.5 to 2.9)
Admit to ICU	6 (0.6)	2 (1.4)	5 (13.5)	13 (1.2)	−3.4 (−3.2 to −1.6)	−12.9 (−25.3 to 0.4)
Admit status unknown	11 (1.2)	3 (1.7)	0 (0.0)	14 (1.2)	−1.0 (−3.9 to 1.9)	1.2 (−0.7 to 3.0)

Abbreviations: ACE, angiotensin-converting-enzyme; Anti-H2, histamine type-2 receptor antagonists; ED, emergency department; ICU, intensive care unit; MAOi, monoamine oxidase inhibitor; NA, not applicable; NSAID, nonsteroidal anti-inflammatory drug.

NOTE. Patients who received 1 dose of pre-ED epinephrine are the reference group.

[a]Significant CI.

Table 2
Factors Associated With 2 or More Prehospital Epinephrine Autoinjector Doses

Variables	Univariable (95% CI)	Multivariable (95% CI)
Age at reaction	1.00 (1.00-1.02)[a]	1.01 (1.00-1.01)[a]
Male sex	0.97 (0.93-1.02)	0.98 (0.94-1.02)
Severe reaction	1.13 (1.04-1.22)[a]	1.13 (1.05-1.22)[a]
Outpatient β agonists	1.09 (1.02-1.17)[a]	1.08 (1.01-1.16)[a]

[a]Statistically significant, *P* values less than .05.

Table 3
Factors Associated With Additional Epinephrine in the Emergency Department Among All Patients

Variables	Univariable (95% CI)	Multivariable (95% CI)
Age at reaction	1.00 (0.99-1.01)	1.00 (0.99-1.01)
Male sex	1.03 (0.98-1.08)	1.03 (0.98-1.08)
Severe reaction	1.22 (1.13-1.33)[a]	1.22 (1.12-1.33)[a]
Tree nut trigger	1.09 (1.02-1.16)[a]	1.09 (1.03-1.16)[a]

[a]Statistically significant, *P* values less than .05.

study were known for asthma, and 118 (10.5%) received inhaled β-agonists before coming to the ED. Our analysis revealed that β-agonist use prehospital is associated with 2 or more doses of epinephrine prehospital. The use of inhaled β-agonists likely indicates respiratory distress in patients with food-induced anaphylaxis and asthma. Inhaled β-agonists remain a second-line treatment for anaphylaxis, and should never delay early administration of epinephrine as per guidelines.[15] Early administration of epinephrine within 30 minutes of symptom onset decreases the risk of poor outcomes in patients with anaphylaxis.[16] This is in line with our study. Asthma is a risk factor for severe reactions.[17] These results illustrate that patients known to have asthma should be more vigilantly observed and treated in the hospital.

Hesitancy to administer epinephrine remains an issue prehospital and in the ED. Indeed, it was reported that only 7% of adults and 20% of children use epinephrine in prehospital settings to treat anaphylaxis.[1] Among those with severe reactions assessed in our study, only 50% received additional epinephrine.[18] This suggests that not only are caregivers hesitant to administer epinephrine, but possibly also health care workers. Furthermore, adolescents known for anaphylaxis inconsistently carry EAIs; 1 study reports that 49% never carried their EAI in many locations and 32% never carried it when they were alone.[19] Hence it is crucial to educate patients who are at risk for anaphylaxis to self-carry and promptly administer the EAI to avoid severe/biphasic reactions.[9,20]

Our study has some limitations. Despite being a Canada-wide study, 77.9% of recruited patients were from Quebec. That said, because of the large sample size of our study, we believe that the results remain generalizable. In addition, given that the culprit allergen was on the basis of self-report, clinical history, and physician judgment in the ED, there is a potential for information bias. We were unable to determine the precise allergen in the emergency setting but rather relied on the parent/caregiver report. Furthermore, the C-CARE registry cannot delineate why patients received additional treatments in the ED, whether it be owing to refractory symptoms or biphasic reactions.

In conclusion, a minority of anaphylaxis cases that used prehospital EAIs required additional treatment in the ED, supporting that the practice parameter suggestion of shared decision making works for most patients.

Table 4
Factors Associated With Admission to the Hospital Among All Patients

Variables	Univariable (95% CI)	Multivariable (95% CI)
Age at reaction	1.00 (1.00-1.00)	1.00 (1.00-1.00)
Male sex	1.02 (0.99-1.04)	1.02 (1.00-1.04)
Severe reaction	1.09 (1.05-1.13)[a]	1.09 (1.05-1.12)[a]

[a]Statistically significant, *P* values less than .05.

Disclosures

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