



Original Article

Pediatricians manage anaphylaxis poorly regardless of episode severity

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Abstract ***Background:*** No information exists on how the knowledge or the practice of pediatricians regarding anaphylaxis episodes vary with episode severity. The aim of this study was to assess and compare pediatrician knowledge on the management of mild and severe anaphylaxis using clinical scenarios and to determine factors that affect their decisions. ***Methods:*** A questionnaire consisting of eight questions on the diagnosis and management of anaphylaxis was distributed at two national congresses. A uniform answer box including possible response choices was given below each question, and respondents were asked to check the answers that they thought appropriate. The management of mild and severe anaphylaxis was examined using two clinical case scenarios involving initial treatment, monitoring, and discharge recommendations. ***Results:*** Four hundred and ten questionnaires were analyzed. The percentage of pediatricians who correctly answered all questions on the management of mild and severe anaphylaxis scenarios was 11.3% and 3.2%, respectively. Pediatricians did significantly better with initial treatment, but they were less knowledgeable with respect to observation time and discharge criteria in the mild anaphylaxis case scenario compared with the severe one (both $P < 0.001$). Multiple logistic regression analysis identified only working in an emergency department or intensive care unit as significantly predicting correct diagnosis of anaphylaxis among pediatricians ($P = 0.01$, 95% confidence interval: 0.11–0.57). No pediatrician-related factors predicted physician knowledge on the management of anaphylaxis. ***Conclusions:*** Pediatricians have difficulty with different steps in managing mild and severe anaphylaxis. Their deficiencies in management may result in failure to prevent recurrences of mild anaphylaxis and may increase mortality in severe anaphylaxis.

Key words anaphylaxis, children, management, pediatrician, severity.

Anaphylaxis is an unexpected serious allergic reaction that can progress rapidly and may cause death.^{1–3} Survival depends on timely recognition and proper management,⁴ but variable clinical presentation and the lack of clear definition and a specific marker or test make diagnosis of anaphylaxis difficult for most physicians.^{5,6} In addition to problems in diagnosis, the management of anaphylaxis is usually perceived as treatment of an acute episode, and this is insufficient to prevent future reactions. Long-term management (risk reduction and prevention) should always complement acute anaphylaxis management and is probably the key to good quality of life thereafter. Although the roles of patients and the community in managing anaphylaxis cannot be discounted, the role and the responsibility of physicians always outweigh the other two. Physicians are the determining individuals not only in diagnosis and treatment but also in informing, training, and increasing awareness of anaphylaxis in the patient

and the community.^{1,2} A few prospective studies have assessed the knowledge of senior house officers,⁶ primary care physicians,⁷ and pediatricians⁸ about anaphylaxis and its management based on case-based surveys. To our knowledge, however, there is no published study comparing pediatrician knowledge or practice in addressing anaphylaxis episodes of different severity, although severity is one of the most important factors determining morbidity and mortality in anaphylaxis. Therefore, the primary aim of this study was to assess and compare pediatrician knowledge about the management of mild and severe anaphylaxis using clinical scenarios. The secondary aim was to determine physician-related factors affecting response, such as gender, time working as a physician, title, affiliation at a university hospital, and working in an emergency department (ED) or intensive care unit (ICU).

Methods

There is no recommended or validated survey instrument on the diagnosis and management of anaphylaxis. Therefore, a questionnaire consisting of eight questions was developed by three pediatric allergists and one pediatric emergency care physician. The questionnaire was composed of two parts. The first part

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asked about demographics such as age, sex, duration of practice as a physician, title, affiliation at a university, and working department. The second part included questions on the diagnosis and management of anaphylaxis and absolute indications for epinephrine autoinjector prescription. The diagnosis of anaphylaxis was examined using six short clinical histories. Two other clinical anaphylaxis case scenarios (case 1, mild; case 2, severe anaphylaxis) were prepared to compare the knowledge of physicians on initial treatment (questions 2 and 5), monitoring (questions 3 and 6), and discharge recommendations (questions 4 and 7) in managing mild and severe anaphylaxis (Appendix 1). A position paper of the European Academy of Allergy and Clinical Immunology (EAACI) on anaphylaxis was used in both preparation of all the questions of the study and in definition of correct responses to these questions.² A uniform answer box including the possible response choices was given just below the questions, and respondents were asked to check the ones that they thought appropriate. They were informed that they could check one or more than one choice. The correct concentration (1:1000 or 1:10 000), dose (0.01 mg/kg or 0.001 mg/kg), and route (s.c. or i.m.) of epinephrine injection were queried in the same way for those marking epinephrine as one of the preferred treatments only in question 2.

The participants consisted of attendees of the annual congresses of the Turkish Paediatric Association and the Society of Paediatric Emergency and Intensive Care Medicine, which were held in 2009 in Turkey. The survey instrument was distributed to the participants during the congresses as a printed sheet given out at the registration desk. Questionnaires answered by pediatric allergists were excluded.

Statistical analysis

The Shapiro–Wilk test was used to evaluate normality of distributions. Normally distributed variables are expressed as mean $\pm$ SD. Categorical variables are shown as percentages and were analyzed using the chi-squared test. Within-group comparisons for mild and severe anaphylaxis scenarios were done using the McNemar test. Multiple logistic regression analysis was used to control for all potential confounding factors to determine the predictors of diagnosis and management of anaphylaxis. $P < 0.005$ was considered statistically significant.

Results

We distributed 1000 questionnaires at two congresses and included 410 returned questionnaires in the analysis. Pediatrician demographics are listed in Table 1. Twenty-five pediatricians (6.1%) did not check any options for diagnosis of anaphylaxis. Anaphylaxis scenarios involving the skin and respiratory system, skin and cardiovascular system, and skin and gastrointestinal system were understood by 87.6%, 87.3%, and 86.5% of the pediatricians, respectively. Hypersensitivity scenarios other than anaphylaxis involving only the skin such as pruritus and hyperemia, urticaria and angioedema, and large local reactions were not marked as anaphylaxis by 88.2%, 85.4%, and 89.6% of pediatricians, respectively. As a whole, 87% of the pediatricians diagnosed anaphylaxis correctly (question 1). Fourteen pedi-

Table 1 Physician demographics ($n = 410$)

	<i>n</i> (%)
Female	238 (58)
Age (years) (mean $\pm$ SD)	34.2 $\pm$ 7.4
Duration working as a physician	
<10 years	229 (56.4)
≥ 10 years	177 (43.6)
Title	
General practitioner	22 (5.4)
Resident in pediatrics	178 (43.4)
Pediatrician	210 (51.2)
Affiliation at university	307 (74.9)
Working in ED/ICU	50 (12.2)

ED, emergency department; ICU, intensive care unit.

cians (3.4%) left blank a question about the absolute indications for use of an epinephrine autoinjector (question 8). Twenty-two pediatricians (5.4%) indicated that they would prescribe an epinephrine autoinjector in cases of anaphylaxis to non-steroidal anti-inflammatory drugs (NSAID), and 152 (37.1%) in cases of anaphylaxis to beta-lactam antibiotics. Absolute indications for epinephrine autoinjector prescription according to the 2007 EAACI position paper were known by 59.5%.² The correct concentration and dosage of epinephrine were known by 80.2% of pediatricians. Forty-six percent of pediatricians preferred the i.m. route, whereas 39.4% preferred the s.c. route for epinephrine injection. Forty-eight percent of physicians who chose epinephrine as the initial treatment gave correct answers for both the route and dose of the epinephrine.

Answers on initial treatment, monitoring, and discharge recommendations by pediatricians for mild (case 1) and severe (case 2) anaphylaxis scenarios are given in Table 2. The percentage of pediatricians who correctly answered all questions on the management (initial treatment, monitoring, and discharge criteria) of mild and severe anaphylaxis scenarios was 11.3% and 3.2%, respectively. Pediatricians did significantly better in initial treatment ($P < 0.001$) but were less knowledgeable with respect to observation time ($P < 0.001$) and discharge criteria ($P < 0.001$) for the mild anaphylaxis case scenario compared with the severe one (Table 2). Seventy-five percent of pediatricians did not indicate that they would give a second dose of epinephrine in case 2, in which the patient did not respond to the first dose of epinephrine and was described as in anaphylactic shock. Sixty-two percent of pediatricians who would not give a second dose of epinephrine in the severe anaphylaxis case checked prednisolone and/or antihistamine instead as the treatment choice. Multiple logistic regression analysis identified only working in an ED or ICU as significantly predicting correct diagnosis of anaphylaxis ($P = 0.01$; 95% confidence interval: 0.11–0.57). Age, sex, duration of experience as a physician, title, working at an ED or ICU or at a university hospital did not predict physician knowledge on initial treatment, monitoring, and discharge recommendations for anaphylaxis.

Discussion

This study compared the knowledge of physicians on the management of anaphylaxis of differing severity using case-based

Table 2 Answers for the management of mild and severe anaphylaxis cases

	Case 1 Mild anaphylaxis (food)	Case 2 Severe anaphylaxis (drug)
Questions 2 and 5.		
What is the most appropriate treatment at this moment for this patient? (%)		
Oxygen	100	100
i.v. fluid	0.0	100
Normal saline	–	73.6
Dextrose	–	1.0
Mixed fluid	–	25.4
Epinephrine	85.8	24.4
Prednisolone ± antihistamine	13.7	59.8
Salbutamol	84.2	0.0
Inotropes	0.0	5.7
Questions 3 and 6.		
How long would you monitor this patient? (%)		
<4 h	14.7	3.0
6–8 h	43.8	7.9
24 h	41.5	89.1
Questions 4 and 7.		
Which of the following would you recommend for this patient before discharge? (%)		
Allergen elimination	100	100
Prednisolone and antihistamine	100	100
Epinephrine autoinjector	40.3	38.4
Referral to an allergist	100	100

Bold, correct answers.

scenarios. Previous reports investigating the knowledge of physicians on the management of anaphylaxis used only case scenarios with either mild or severe anaphylaxis.^{6–8} The present study shows that pediatricians are generally good at diagnosis but poor at management of anaphylaxis, regardless of the severity of the episode.

Diagnosing anaphylaxis is the key to treatment. It seems that the present participants did better than those in other studies with respect to the diagnosis of anaphylaxis.^{7,8} We think that the anaphylaxis sessions in the two congresses might have influenced this result, although we cannot be sure whether all participants attended these sessions.

In the present study, most of the participants were specialists or residents in pediatrics. Although they seemed to do significantly better in the management of mild anaphylaxis compared with severe anaphylaxis, as a whole, their knowledge was far below what might be expected. Pediatricians were found to correctly prefer oxygen and epinephrine for the initial treatment of mild anaphylaxis, but fewer than half knew the correct dose and route for epinephrine. Also, in other reports, the percentage of physicians who would use epinephrine as the initial treatment in anaphylaxis ranged between 24% and 72%.^{7–9} Moreover, pediatricians were found to have relatively inadequate knowledge of the observation period and discharge recommendations. Similarly, Wang *et al.* found that 38% of pediatricians thought that an observation period <4 h is sufficient after the initial treatment.⁷ Worse still, Krugman *et al.* reported that 70% of pediatricians seemed to think that an observation period of 30 min is sufficient for mild anaphylaxis.⁸ The EAACI, however, recommends at least 6–8 h of observation for children with anaphylaxis involv-

ing the respiratory system.² Interestingly, in the present study, the proportion of pediatricians who elected to observe the mild anaphylaxis patient longer than needed was very close to the proportion of pediatricians who chose the recommended observation period. Although 24 h of monitoring is not necessarily wrong, a longer observation period certainly increases the length of ED stay and the costs. We think that this finding may be a result of lack of confidence of pediatricians.

Severe anaphylaxis with cutaneous and cardiovascular findings such as hypotension is usually easy to diagnose but more difficult to manage. Unfortunately, fewer than one-fourth of the pediatricians thought to give a second dose of epinephrine in the case of a patient who was described as hypotensive with poor peripheral circulation despite the first dose of i.m. epinephrine. Instead of repeating the epinephrine injection, more than two-thirds of the pediatricians chose prednisolone and antihistamine at this stage. The position paper states that the dosage of adrenaline can be repeated at short intervals until the patient's condition stabilizes,² but all of the physicians marked that they would give i.v. fluid to this patient. There is only one study in which an adult with anaphylactic shock was described; in that study all senior house officers starting accident and emergency posts answered that they would initially treat the patient with epinephrine, but 55% would do so by the incorrect route.⁶ Previously, better evidence for poor management of severe anaphylaxis in real life was documented by Pumphrey.¹⁰ In that report, Pumphrey noted that epinephrine was used before arrest in only 14% of fatal anaphylactic reactions. Thus, we think that inadequate knowledge of the management of severe anaphylaxis and/or fear of side-effects are the main reasons why pediatricians prefer systemic

corticosteroids with or without antihistamine treatment instead of giving or repeating epinephrine.¹¹ There are no absolute contraindications for epinephrine treatment, however, in children, in contrast to adults, in whom coronary heart disease and cardiac arrhythmias are frequent.^{1,2}

Discharge recommendations for anaphylaxis should address prevention of recurrence and self-preparedness for acute management of future inevitable episodes, as well as oral corticosteroid and antihistamine treatment for 72 h and referral to an allergist. The present participants did excellently in all discharge recommendations except for that for epinephrine autoinjector in both mild and severe anaphylaxis cases. Absolute indications for epinephrine autoinjector prescription in children were reported as previous respiratory or cardiovascular reaction to food, insect sting, or latex; exercise-induced anaphylaxis; idiopathic anaphylaxis; and food allergy with coexisting persistent asthma.² Although almost two-thirds of the participants knew the absolute indications for epinephrine autoinjector prescription, less than half prescribed it to children who experienced anaphylaxis with food in a case-based survey.

Certainly, the present study has some limitations. The major limitation is that all of the prepared questions and their correct answers were based on only the EAACI position paper.² There was a possibility, however, that participants may have answered these questions based on the knowledge of other guidelines.^{1,12–14} Given that the available guidelines are not consistent with each other for certain subjects such as prescription indications for epinephrine autoinjector in anaphylaxis, this discrepancy may have influenced the results. Neither the reference guide, the 2007 EAACI position paper,² nor the recent EAACI position paper scheduled for publication late in 2014,¹⁵ pronounce drug-induced anaphylaxis as an absolute or relative indication for epinephrine autoinjector prescription, but this issue is not clearly described in the other guidelines.^{1,12–14} As a consequence, the aforementioned discrepancies among guidelines may have a significant impact on both the attitudes/behaviors of physicians towards epinephrine autoinjector prescription for patients with anaphylaxis, and the present results.¹⁶ Although the intent was to investigate the knowledge of physicians on anaphylaxis as a whole, including diagnostic criteria, initial treatment, further treatment, and discharge recommendations, using case-based scenarios, there may be other points that we have not investigated. Also, the present study was a questionnaire-based survey, which may not directly reflect the pediatricians' real-life practice.

Physicians have difficulty in different steps in the management of mild and severe anaphylaxis. In cases of mild anaphylaxis, they often either do not grant enough importance to or they neglect the observation period and discharge recommendations, which are important to prevent recurrence after the patient recovers following initial treatment. In contrast, in severe anaphylaxis, their knowledge was very inadequate even with respect to initial management, which certainly has an effect on mortality. Finally, no physician-related factors were found to predict knowledge on the management of anaphylaxis. This is important because it

points to a basic shortage of and necessity for continuing medical education for physicians in the management of anaphylaxis regardless of the physician's duration of practice, title, affiliation at a university hospital, or working in an ED or ICU.

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Appendix 1

Questionnaire

Question 1. Tick the cases that you would diagnose as anaphylaxis

- ✓ Urticaria, swelling of lips and wheezing sound in an 8-month-old baby 10 min after being fed by formula
- ✓ Pruritus and hyperemia around the mouth in a 5-year-old child 5 min after eating hazelnuts
- ✓ Generalized urticarial rash, vomiting and abdominal cramps in a 7-year-old boy 20 min after penicillin injection
- ✓ Swelling of eyelids and generalized urticarial rash in a 2-year-old girl 1 h after drinking milk
- ✓ Hypotension in a 6-year-old boy who developed flushing and fainted 5 min after eating peanuts
- 10 cm swelling and pruritus around stung region in a 10-year-old girl 30 min after a bee-sting

Case 1 (for questions 2–4)

Eight-month-old boy was brought to pediatric ED with generalized flushing, edema of the lips 20 min after he ate scrambled eggs at breakfast.

On arrival to the ED, he was alert. Vital signs were T 37°C, HR 136 beats/min, systolic BP 90 mmHg, RR 48/min, SpO₂ in room air 93%.

He had mild wheezing.

Case 2 (for questions 5–7)

An 8-year-old boy was diagnosed as having pharyngitis and was treated with benzathine penicillin. Immediately after injection, he developed generalized pruritus, hives, and cough, near syncope. Family physician gave 0.3 mg 1 : 1000 epinephrine i.m. Then, he was transferred to ED by ambulance. On arrival to the ED, he was alert with no apparent respiratory distress but in prostration. Vital signs were T 37°C, HR 150/min, systolic BP 70 mmHg, RR 32/min, SpO₂ in room air 93%. He had generalized urticarial rash, weak central pulse and prolonged capillary refill time. Respiratory sounds were normal.

Question 8. Tick the situations with absolute indication of adrenaline autoinjector prescription.

- ✓ Anaphylaxis with food, venom or latex
- ✓ Anaphylaxis with trace amount of food in a patient with persistent asthma
- ✓ Anaphylaxis with beta-lactam antibiotics
- ✓ Exercise-induced anaphylaxis
- ✓ Idiopathic anaphylaxis
- Anaphylaxis with NSAID

Questions 2–4 and 5–7 are related to initial treatment, monitoring and discharge recommendations. ✓, correct answer. BP, blood pressure; ED, emergency department; HR, heart rate; i.m., intramuscular; RR, respiratory rate; SpO₂, saturation of oxygen; T, temperature.