



BRIEF COMMUNICATION

Severe Anaphylaxis in Children: A Single-center Experience



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1. Introduction

Anaphylaxis involves several organ systems and evolves dynamically, that is, it may spontaneously stop with mild symptoms or rapidly progress to life-threatening laryngeal edema or shock. It is not possible to determine the severity of the attack in advance. Severe anaphylaxis deserves special attention because of its increased risk of morbidity and mortality. Although not as much as anaphylaxis in general,^{1–3} reports of severe anaphylaxis have been increasing in number with time. For this reason our study aimed to investigate the demographics, atopic status, etiological factors, clinical properties, treatment, and follow-up of patients who presented with severe anaphylaxis.

2. Methods

We conducted a retrospective medical chart review for a 10-year period between January 2002 and September 2012. The patients' files were separately reviewed by two

pediatric allergists. Children whose anaphylaxis diagnosis was confirmed by the two allergists and who fulfilled the criteria for severe anaphylaxis according to the position paper of the European Academy of Allergology and Clinical Immunology⁴ were included in the final analysis. Demographics, triggers, number of previous anaphylaxis episodes, clinical manifestations and involved systems, the interval between exposure and the onset of anaphylaxis, treatment of the acute episode, comorbid diseases, and long-term management were recorded. Etiologic factors were determined by history and skin prick and/or intradermal tests with the suspected allergens mentioned in the history.

The study was approved by the Ethics Committee of Gazi University, Ankara, Turkey.

3. Results

During a period of 10 years in the Gazi University Pediatric Allergy and Asthma Department, 34 (25%) of 136 cases were diagnosed as severe anaphylaxis. Twenty-one of these patients were male (61.8%), and the mean age was 79.0 ± 61.7 months. Drugs were the most common etiological agents (61.8%; [Table 1](#)). In six cases (17.6%) there was a comorbidity of atopic disease (3 asthma cases, 2 allergic rhinitis cases, and 2 atopic eczema cases). Five

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cases had a history of type 1 food allergy, four cases had a history of type 1 drug allergy, and four cases had an anaphylaxis attack previously (foods were the etiological agents in all previous attacks of anaphylaxis). The analysis of the reported interval between exposure to the causative agent and the appearance of the first symptom showed that in 20 cases (58.8%) the reaction was immediate (1–5 minutes), in eight cases (23.5%) the reaction within 5–30 minutes, and in six cases (17.6%) the reaction was within 30–120 minutes. Respiratory symptoms (25 cases, 73.5%) were the most common symptoms observed, followed by cardiovascular and cutaneous symptoms (23 cases, 67.6%; Table 1). Hypotension was detected in 21 of 25 patients whose blood pressure was measured. Five cases

(14.7%) had a cardiac arrest. Twelve cases (35.2%) had stridor, 17 cases (50%) had cyanosis, and 17 cases (50%) had syncope. The youngest patient who had a cardiac arrest was 30 months old and the oldest patient was 72 months old. All were male, and the reaction occurred within the first 5 minutes after exposure. The etiological agent was ceftriaxone in three cases, penicillin in one case, and a general anesthetic agent in one case. Detailed information was available in three cases that had cardiac arrest. Two patients responded to cardiopulmonary resuscitation within 5 minutes (etiological agents were ceftriaxone in one case and general anesthetic agent in the other case). The other case was treated with cardiopulmonary resuscitation for 15 minutes, had been intubated, and taken to the intensive care unit (etiological drug was ceftriaxone). After this event, the child recovered but had neurological problems. Treatment of anaphylaxis in the medical facility for those 30 cases whose medical records have been accessed included antihistamines in 26 patients (86.6%), corticosteroids in 27 patients (90%), epinephrine in 20 patients (66.6%), oxygen in 28 patients (93.3%), IV fluid in 23 patients (76.6%), and a β -2 agonist in five patients (16.6%). Four patients (11.7%) needed IM adrenaline twice. Six patients (17.6%) were observed in the emergency room for more than 24 hours, five patients (14.7%) were followed up in the intensive care unit, and two patients were hospitalized for underlying systemic disease. Thirteen of 34 cases were prescribed an epinephrine autoinjector: six for food (46.1%), six for hymenoptera venom (46.1%), and one for exercise-induced (7.8%) anaphylaxis. Thirty-two patients could be contacted for follow-up. Two had experienced a second episode after diagnosis (6.2%). Although an epinephrine autoinjector was prescribed and patients/parents were trained in their use previously, only one of them had used the epinephrine self-administration device (Epipen) at the time of the reaction.

Table 1 Causes, symptoms, and signs of severe anaphylaxis ($n = 34$).

	<i>n</i> (%)	Specific agent (<i>n</i>)
Causative agent		
Drugs	21 (61.8)	Antibiotics (11) Cephalosporins (6) Penicillin (4) Vancomycin (1) NSAIDs (3) Enzyme replacement therapy (3) α -L-iduronate (1) Idursulfase (1) Galsulfase (1) General anesthetic agents (3) Insulin (1)
Food	6 (17.6)	Hen's egg (3) Cow's milk (2) Peach (1)
Venom	6 (17.6)	Vespid (4) Aphids (2)
Exercise-induced	1 (2.9)	
Symptom or sign		
Respiratory	25 (73.5)	
Dyspnea	6 (17.6)	
Stridor	12 (35.3)	
Wheezing	2 (5.9)	
Cough	6 (17.6)	
Rhinorrhea	2 (5.9)	
Hoarseness	2 (5.9)	
Cyanosis	17 (50)	
Cardiovascular	23 (67.6)	
Hypotension	21/25 (84)*	
Syncope	17 (50)	
Arrest	5 (14.7)	
Cutaneous	23 (67.6)	
Angioedema	17 (50)	
Urticaria	18 (52.9)	
Flushing	6 (17.6)	
Pruritus	4 (11.8)	
Gastrointestinal	4 (11.8)	
Persistent vomiting	4 (11.8)	

NSAIDs = non-steroidal anti-inflammatory drugs.

* Only 25 of the cases whose blood pressure was measured.

4. Discussion

This study showed that drugs were the major etiological factor in severe anaphylaxis cases, and symptoms and signs occurred immediately after contact with the suspicious agent. Although the most frequent symptoms/signs involved were respiratory, hypotension was detected in a remarkable percentage of patients with severe anaphylaxis.

In retrospective studies of anaphylaxis cases, cutaneous symptoms/signs were the most common during the reaction. Respiratory and cardiovascular symptoms were generally observed less often than cutaneous symptoms/signs.^{1–3} However, Stoevesandt et al⁵ reported that the absence of urticaria and angioedema was frequently associated with venom-induced severe anaphylaxis. In our study, respiratory symptoms/signs were most prominent in cases of severe anaphylaxis. Cardiovascular and cutaneous symptoms/signs followed respiratory symptoms/signs. Also, more than 80% of our patients were reported to be hypotensive, which is an important sign. It shows the severity of the reaction and is an alarming signal for morbidity and mortality from anaphylaxis. Renaudin et al⁶ analyzed 333 cases who were diagnosed with drug-induced severe anaphylaxis. Among those, 76.6% had anaphylactic shock.

These results illustrate that hypotension is a common finding in severe anaphylaxis.

Pumphrey⁷ studied the average time from contact with the trigger to onset of cardiopulmonary arrest in severe anaphylaxis that resulted in death. This time was reported to be 30 minutes in food-induced, 15 minutes in venom-induced, and 5 minutes in drug-induced anaphylaxis. Stoevesandt et al⁵ found a significant association between the onset of the reaction and the severity of venom-induced anaphylaxis, that is, if the reaction starts within the first 5 minutes, the episode is more severe. In our study, two-thirds of patients with severe anaphylaxis had reactions that developed within the first 5 minutes.

Failure to measure serum tryptase level in patients diagnosed with severe anaphylaxis is a limitation of this study. It has been shown that a high serum tryptase level is a risk factor in severe anaphylaxis.⁵ Moreover, the small number of patients and the retrospective nature of the study are additional limitations.

In conclusion, drugs are the major triggers of severe anaphylaxis. The reaction occurs immediately after contact with the etiological factor. The most frequent symptoms/signs involve the respiratory system followed by the cardiovascular system and cutaneous.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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