

Epinephrine Can Save Lives. Anaphylaxis, always a Challenge: A Therapeutic Approach on Children

Sur Genel^{1,2}, Sur Maria¹, Kudor-Szabadi Liana¹, Sur Lucia¹, Sur Daniel¹ and Samasca Gabriel^{1,2*}

¹University of Medicine and Pharmacy, Iuliu Hatieganu, Cluj-Napoca, Romania

²Emergency Clinical Hospital for Children, Cluj-Napoca, Romania

Abstract

Correct treatment of anaphylaxis in emergency events is a key point to prevent death and subsequent events. Anaphylaxis can be quickly diagnosed if we recognize respiratory and circulatory manifestations and we correctly assess mental status. The first and most important treatment is epinephrine. After successful therapy, the clinician's attention must be directed toward preventing recurrences- biphasic anaphylaxis and to elucidate the causes. The patient will need to be explained the importance of preventing relapse and needs to be equipped with epinephrine, which to use in critical situations. There are differences concerning therapeutic approach, recognition of symptoms and patient education, depending on physician's experience, on patient's education level and on socio-economic level of their country.

Introduction

Anaphylaxis is a major emergency, it may have an unpredictable evolution, may progress rapidly to a fatal outcome if we don't establish the correct diagnosis, that has to be followed by rapid treatment measures.

Anaphylaxis responds promptly to treatment with epinephrine, but new episodes may occur, or at least one new episode, so-called biphasic anaphylaxis, and clinicians always have to consider this situation. From an epidemiological point of view, in most countries there is no clear evidence of cases of anaphylaxis.

Correct management of anaphylaxis requires an accurate treatment of the first episode, identifying causes and preventing future episodes [1-9].

Epidemiology of Anaphylaxis

Anaphylaxis is defined as an acute disease (minutes or hours after exposure to the allergen) with skin manifestations (general hives, itch or flushing, swollen lips-tongue-uvula), respiratory manifestations (dyspnoea, wheezing, bronchospasm, stridor, reduced peak expiratory flow, hypoxemia), decreased blood pressure and other symptoms associated with organ dysfunction (collapse, syncope, hypotonia) [10-14]. These events occur after the contact with an allergen due to mast cell degranulation, after the circulation of preformed mediators (histamine) and newly formed (leukotrienes) [15-18]. The incidence of anaphylaxis is estimated at 30 cases per 100.000 patients per year. Regarding mortality due to anaphylaxis, there is no rigorous evidence. If we consider the prescribed epinephrine, the incidence of the child would be 1-5 cases per 1000 patients [19-22].

It is believed that currently there is a growing tendency of anaphylaxis cases, due to widespread use of products with allergenic potential. During a year, at the Children's Hospital from Cluj have been investigated for allergic manifestations 1180 children, of whom 533 were positive. The largest number were positive to mites (232 patients), other 140 patients to animal hair, 85 children to milk, 59 to pollen, 50 to milk proteins, 25 to eggs, 26 to molds and the rest to vegetables and fruits.

Anaphylaxis was observed in 3 children, of whom one died the patient arrived too late to the hospital and the treatment was no longer

efficient. In the U.S. it is estimated that food is responsible for about 30.000 cases of anaphylaxis per year, with 2.000 hospitalizations and 200 deaths. For children, the risk of anaphylaxis is 1 in 2 years for foods with 0.6 to 5 % mortality per episode.

Clinical Diagnosis

Anaphylactic events are easily recognized by an experienced physician. Clinical manifestations occur in 1-15 minutes after exposure to allergen. In some cases, they can occur 30 minutes to an hour after exposure. The patient is unwell, becomes agitated, complains of tachycardia and tachypnea. Other symptoms like tingling sensations, itch and flushed skin, throbbing in the ears, coughing, sneezing, hives and swelling (angioedema) may occur. Breathing may become difficult and wheezing may occur due to upper airways constriction and swelling. An anaphylactic reaction may progress so rapidly that it leads to collapse, cessation of breathing and loss of consciousness within 1-2 min. The reaction may be fatal unless treatment is applied immediately.

At presentation in the emergency room, anaphylaxis may not be recognised if it is triggered by a new agent, if it is an individual's first episode, or if it's an infant or a young child, or in an aphonic, dyspnoeic or unconscious individual.

The diagnosis of anaphylaxis is mainly based on the clinical history, and clinical criteria.

An anaphylactic episode is defined not only by the simultaneous involvement of two or more organs or systems, but mainly by the involvement of vital systems.

Anaphylaxis can present in various ways, in the major symptoms

***Corresponding author:** Gabriel Samaşca, Department of Immunology, Croitorilor Street, 19-21 No, Iuliu Hatieganu, University of Medicine and Pharmacy, Cluj-Napoca, Romania, E-mail: Gabriel.Samasca@umfcluj.ro

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60 % has to do with the skin (hive and flushing), but there can also be serious respiratory or cardiovascular failure, difficulty in breathing, swollen and tingling lips or a fall in a blood pressure leading to dizziness, nausea or pallor. As clinical manifestations can change, during a single episode at onset, a careful observation of the patient imposes.

The clinical presentation of anaphylaxis may vary: from one episode to another, with the time from to exposure to the trigger, the onset of symptoms, and the severity of symptoms [23-25].

Differential Diagnosis

When there is a history of recent exposure to a known allergen, anaphylaxis diagnosis is easy.

When cardiovascular and gastrointestinal manifestations predominate, diagnosis is more difficult.

Respiratory pathology

Respiratory distress syndrome; recent inhalation of foreign antibodies.

Neurological

Epileptic syndrome with hypotonia and loss of consciousness.

Flushing syndromes

Various agents have been involved in causing flushing: angiotensine converting enzyme inhibitors (histamine, kallikrein, nicotine) and carcinoid syndrome (flushing, diarrhea, colic and wheezing); medullar carcinoma of the thyroid is another important condition (persistent flushing of the face, hands and feet). Flushing syndrome is wet and dry. In the wet form caused by the postmenopausal state, sweating accompanies the flushing because of sympathetic cholinergic stimulation of the sweat gland. In carcinoid syndrome, dry flushing appears because sweat glands are not activated. In alcohol ingestion, flushing can also be present, especially within Asian people, who lack the aldehyde dehydrogenase 2 enzyme. Alcohol can also lead to flushing in patients with Hodgkin's disease, hypereosinophilia syndrome and splenectomy.

Restaurant syndrome

Scombroid-fish poisoning due to histamine has been described in adults and children (fish colonized by enterobacteria - *Klebsiella oxytoca* and *Morganella morgani*) can contain histamine derived from histidine through bacterial action. The Chinese restaurant syndrome caused by monosodium glutamate in foods may also provoke flushing, headache and abdominal symptoms.

Sulphites from preservatives in gelatin, sauces, wine, fruit juices, cheese, mollusks can cause the same symptoms as monosodium glutamate.

Vasovagal reactions are a reflex of the involuntary nervous system causing bradycardia, hypotension and vasodilatation. Vasovagal syndromes are generally caused by physical or emotional stress and characterized by pallor, asthenia, nausea, hypotension, vomiting and profuse sweating.

Excess of endogenous histamine production

The Vancomycin induced red man syndrome, mediated by histamine systemic mastocytosis can determinate anaphylactic acute syndrome.

Promyelocytic leukemia and basophilic leukemia treated with Treonin can also cause anaphylactic reaction.

Echinococcal cysts may be a possible cause of anaphylactic episode via histamine.

Psychogenic conditions

Munchausen syndrome, globus hystericus and panic attacks can imitate anaphylactic symptoms.

Another allergic manifestation

Hereditary angioedema can mimic anaphylactic attacks. These patients have usually had episodes triggered by trivial traumas such as oral or dental manipulations. Prompt recognition of this attacks may be critical, as long as oedema of the tongue and upper airways is the cause of death in 15-30 % of this patients.

The systemic capillary leak syndrome, a severe sometimes fatal idiopathic condition with shock and massive edema, often after a nonspecific prodrome of weakness, fatigue, and myalgias is also one of the differential diagnosis.

Gleich's syndrome is characterized by episodic urticaria/angioedema, hypereosinophilia and elevation of immunoglobulin M [26-32].

Laboratory Diagnosis

The diagnosis is primarily clinical but laboratory tests may bring additional information: IgE mediated anaphylaxis. More valuable is the measurement of metabolites such as: tryptase, plasma and urinary Histamine [33-36].

Emergency Treatment of Anaphylaxis

The elements of the intervention to be rapidly activated can be summarized in the mnemonic airway patency, breathing, circulation and mental status (ABCM). The patient must be kept horizontal, with raised legs, to promote the perfusion of vital organs [37-39].

Epinephrine must be injected intramuscular (s.c is not recommended because local vasoconstriction can reduce deposition. The substance should be injected intramuscularly in the thigh, on the lateral part of the quadriceps or in the deltoid muscle.

The dose is 0.01mg/kg of aqueous Epinephrine 1:100 (up to 0.5 ml to be repeated if necessary after 5-30 minutes).

If the patient's weight is unknown, an approximate dosage is 50 µg (50 µg-0.05 ml for infants less than 6 months; 120 µg-0.12 ml for children between 6 month to 6 years; 250 µg-0.25 ml from 6 to 12 years; 500 µg-0.5 ml for children older than 12 years).

During the administration of Epinephrine, vital signs-cardiac activity, respiratory function and blood pressure should be continuously monitored and airways patency should be continuously maintained to prevent rapid worsening.

If symptoms do not decrease:

1. Repeat Epinephrine after 5 minutes;
2. Establish a venous access; in hypotension rapidly administer isotonic saline solution, 20-30 ml/h in the first hour;
3. If hypotension persists rapid diffusion of volume expanders;
4. Administer oxygen: 5-8 l/min;

5. Administer support drugs: antihistamines (Clorpheniramine), bronchodilators (Salbutamol), corticosteroids (Hydrocortisone), glucagons, Dopamine.

Antihistamines are indicated for treatment of pruritus and urticaria. Clorpheniramine is used in a dose of 1 mg/kilo; other antihistamines: Levocetirizine, Desloratadine.

Salbutamol can be used for relief of bronchospasm.

Methylprednisolone is used in a dose of 1-2 mg/day i.v.

Biphasic Anaphylaxis can be developed after as many 20 % of anaphylaxis. The interval between the first anaphylactic reaction and the subsequent fatal or near fatal anaphylactic episode can last between 2 to 12 hours, and no specific symptom is predictive of recurrences. One Epinephrine injection is similar to first episode ?? Systemic corticosteroids are unable to prevent recurrence [40-44].

Conclusion

The emergency department is very important for anaphylaxis treatment and the prevention of subsequent recurrences.

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