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PEDIATRIC ANAPHYLAXIS: NARRATIVE REVIEW

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ABSTRACT Anaphylaxis is a severe, rapidly occurring allergic reaction that can be fatal. Diagnosis relies on clinical signs and symptom details, involving skin or mucosal symptoms, respiratory compromise, and reduced blood pressure. Anaphylaxis can manifest in various ways, and immediate administration of epinephrine is crucial. The primary pharmacologic treatment is epinephrine, administered as an intramuscular injection. Depending on the patient's age and weight, various doses are recommended. Other adjunctive treatments include antihistamines, bronchodilators, and glucocorticoids, but they should not replace epinephrine. Refractory anaphylaxis, unresponsive to initial treatment, poses challenges and may require additional interventions such as vasopressors or ECMO. Recognizing and treating anaphylaxis promptly is vital to save lives.

KEYWORDS : Anaphylaxis, Epinephrine, Allergic reaction.

INTRODUCTION

Anaphylaxis in children is a critical medical emergency necessitating immediate diagnosis and intervention. This condition, characterized by a sudden onset of potentially life-threatening symptoms affecting multiple body systems, demands urgent attention. However, diagnosing and managing anaphylaxis in children involves a multifaceted approach. Not only must healthcare professionals confirm the diagnosis and identify the causative factors, but they should also evaluate potential contributors, such as concurrent medications and medical conditions. In many cases, referral to an allergy/immunology specialist is recommended to ensure a comprehensive assessment and to address the long-term management and prevention of recurrent anaphylactic episodes in pediatric patients. The nature and chronology of anaphylactic events are key considerations, and understanding exposures and activities in the patient's history plays a crucial role in effective diagnosis and treatment. Additionally, the presence of comorbidities and concurrent medications should be evaluated to improve patient care and minimize the risk of severe or fatal anaphylaxis in children.

Methods

To conduct a narrative review on pediatric anaphylaxis, a comprehensive search strategy was developed in collaboration with a research librarian. Systematic searches were performed in electronic databases, including PubMed, Embase, and Cochrane Library, using a combination of keywords related to pediatric anaphylaxis, diagnosis, treatment, risk factors, and prevention. Additionally, manual searches were conducted in the reference lists of included articles and relevant reviews to ensure the inclusion of all pertinent studies. Studies involving pediatric patients with anaphylaxis and focusing on management strategies, diagnosis, treatment, and prevention were considered.

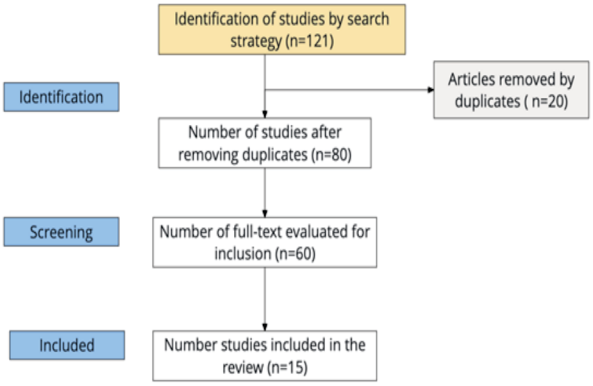

Figure 1. PRISMA.

After identifying potentially eligible studies, full-text articles were assessed for inclusion in the review. A narrative synthesis of the findings was conducted to provide an overview of the various approaches and strategies employed in the management of pediatric anaphylaxis. The strength of the evidence and the quality of the studies were considered in the interpretation of the results. Fifteen relevant references were included, covering various dimensions of pediatric anaphylaxis, including diagnosis, treatment, risk factors, and prevention, to offer a comprehensive insight into this condition in children.

Diagnosis Acute

The estimated lifetime prevalence of anaphylaxis in industrialized countries ranges from 0.05% to 2% within the general population, with increasing incidence rates. In the United States, strict clinical diagnostic criteria reveal a minimum lifetime prevalence of 1.6% (2)

Anaphylaxis is defined as a rapid-onset, severe allergic or hypersensitivity reaction that can lead to death (3).

Diagnosing anaphylaxis relies primarily on clinical signs, acute episode details, and antecedent activities. Diagnostic criteria published by experts include three scenarios to identify anaphylaxis. These criteria involve skin or mucosal symptoms, respiratory compromise, and reduced blood pressure. A second set of criteria was proposed by the World Allergy Organization in 2020, focusing on acute illness onset involving the skin or mucosal tissues and respiratory or circulatory compromise, or laryngeal involvement following exposure to a known allergen (4).

Anaphylaxis may manifest through various symptoms and signs, including skin and mucosal symptoms (up to 90% occurrence), respiratory symptoms (up to 85% occurrence), gastrointestinal symptoms (up to 45% occurrence), and cardiovascular symptoms (up to 45% occurrence). Anaphylaxis is unpredictable and can range from mild, self-resolving episodes to severe, life-threatening events. Immediate administration of epinephrine is crucial to prevent progression to life-threatening manifestations. While rare, death from anaphylaxis is usually due to upper or lower airway obstruction or cardiovascular collapse and can occur within minutes of symptom onset. Anaphylaxis typically exhibits a rapid onset within seconds to minutes of exposure to a causative agent, followed by the evolution and eventual resolution of symptoms. Episodes may be uniphasic (most common), biphasic (in about 5% of cases), or protracted, and occasionally refractory (5).

Certain comorbidities (e.g., asthma, cardiovascular disease),

concurrent medications (e.g., beta-blockers, ACE inhibitors), and external factors (e.g., acute infection, exercise) can influence the severity of anaphylactic reactions. While anaphylaxis is clinically diagnosed, supportive laboratory tests include measuring total tryptase or plasma histamine levels. These tests, if done within hours of symptom onset, can help retrospectively confirm the diagnosis.

Around 40 other diseases and conditions should be considered in the differential diagnosis of anaphylaxis, with common differentials including acute generalized urticaria/angioedema, acute asthma exacerbations, syncope, and anxiety/panic attacks. This review underscores the critical importance of promptly recognizing and treating anaphylaxis, a condition with variable presentations and potentially fatal outcomes, thereby saving lives and preventing complications.

Immediate Management

Immediate management of anaphylaxis is paramount, given its potential to lead to rapid respiratory or cardiac failure [6]. Timely intervention is critical as anaphylaxis appears to be most responsive to treatment in its early stages [7]. Key steps in anaphylaxis management involve the identification and removal of triggers, calling for assistance, and the immediate administration of epinephrine. Correct patient positioning is vital, and supplemental oxygen, as well as fluid resuscitation, should be initiated as part of the management plan. In cases of upper airway obstruction, prompt intervention such as intubation or even an emergency cricothyroidotomy may be necessary. Ensuring access to intravenous fluids is crucial as anaphylaxis can lead to rapid fluid shifts [6]. Special considerations apply to pregnant patients, including positioning on the left side and maintaining systolic blood pressure [7]. In the event of anaphylaxis, a coordinated, rapid response that focuses on airway, breathing, circulation, and mental status is essential [6].

Pharmacologic Treatments

Anaphylaxis is a severe and potentially life-threatening allergic reaction that can occur suddenly and unpredictably in response to allergens [7]. The primary pharmacologic treatment for anaphylaxis is epinephrine [8]. It is the first and most critical intervention to counteract the symptoms of anaphylaxis, such as airway obstruction, hypotension, and shock [9].

Epinephrine, also known as adrenaline, is administered as soon as anaphylaxis is recognized to prevent the progression to life-threatening symptoms [10]. It is available in various concentrations, but the recommended dilution for intramuscular (IM) injection is 1 mg/mL [10]. The proper route of administration for initial treatment is IM injection into the mid-outer thigh (vastus lateralis muscle) [10].

The dosing of epinephrine depends on the patient's age and weight, and it is essential to use the correct concentration to avoid complications [10]. For infants weighing less than 10 kg, an autoinjector with a 0.1 mg dose can be used, or 0.1 mL of the 1 mg/mL solution may be drawn up [10]. Infants and children weighing from 10 kg to 25 kg can receive 0.15 mg by autoinjector or 0.15 mL of the 1 mg/mL solution [10]. Patients weighing more than 25 kg but less than 50 kg can be given 0.3 mg by autoinjector or 0.3 mL of the 1 mg/mL solution [10]. Patients weighing over 50 kg can receive 0.5 mg (0.5 mL of the 1 mg/mL solution) [10].

Most patients respond well to a single IM dose of epinephrine, especially if administered promptly after the onset of symptoms [10]. However, for patients who continue to be hypotensive after initial IM epinephrine, intravenous (IV) fluids should be administered, and preparations for an epinephrine solution for slow, continuous infusion should begin [11].

The use of IV bolus epinephrine should be avoided whenever possible due to the associated risks of dosing errors and cardiovascular complications [11]. Intravenous epinephrine should be administered as a slow, continuous infusion if the patient does not respond to IM injections [11]. For adults, the recommended starting dose is 0.1 mcg/kg/minute, with potential increases as needed [11]. In pediatric patients, dosing ranges from 0.1 to 1 mcg/kg/minute, with adjustments made based on the response to treatment [11].

Epinephrine works by addressing various physiological changes that occur during anaphylaxis [12]. It decreases mediator release from mast cells, relieves airway obstruction, and prevents cardiovascular collapse [12]. Its actions include alpha-1-adrenergic effects (increased vasoconstriction and peripheral vascular resistance), beta-1-adrenergic effects (increased inotropy and chronotropy), and beta-2-adrenergic effects (increased bronchodilation and decreased release of inflammatory mediators) [12].

While epinephrine is the primary treatment for anaphylaxis, there are no absolute contraindications to its use [13]. Special consideration should be given to patients with cardiovascular diseases, those taking certain medications (e.g., beta blockers), and individuals with preexisting conditions that might increase the risk of adverse effects [13]. In such cases, clinical judgment and a risk-benefit analysis should guide the decision to use epinephrine [13].

Adjunctive treatments for anaphylaxis include H1 antihistamines, H2 antihistamines, bronchodilators, and glucocorticoids [14]. However, it's essential to note that these should not be used as initial or sole treatments, as they do not address the life-threatening symptoms and complications of anaphylaxis [14]. They can be administered after epinephrine in cases where appropriate [14].

H1 antihistamines can help relieve itching and hives, while H2 antihistamines (when used with H1 antihistamines) may provide additional relief for hives [14]. Bronchodilators are used to treat bronchospasm, and glucocorticoids may be given to reduce the risk of biphasic reactions in severe cases [14]. However, glucocorticoids are not considered a standard treatment for anaphylaxis, and their onset of action is too slow to provide immediate relief [14].

Refractory Anaphylaxis

Refractory anaphylaxis presents a challenge in medical practice, often defined by an inadequate response to initial interventions. When anaphylaxis persists despite appropriate epinephrine dosing and medical management, it is considered refractory. This typically involves the use of three or more doses of epinephrine or the initiation of an intravenous epinephrine infusion. Swift transfer to an intensive care unit is crucial for unresponsive patients. Unfortunately, there is a lack of prospective studies on the optimal management of refractory anaphylaxis. A retrospective review of 11,596 anaphylaxis cases identified 42 instances of refractory anaphylaxis, mainly due to medications, particularly in the perioperative setting, and had a high mortality rate of 26% (14).

Refractory anaphylaxis may require additional vasopressors if hypotension persists despite maximal epinephrine and fluid therapy. Nonadrenergic vasopressors like vasopressin and other adrenergic vasopressors, such as norepinephrine and dopamine, may be considered. Methylene blue, which inhibits nitric oxide synthase and guanylate cyclase, is suggested for profound vasodilation in severe anaphylaxis cases, often in perioperative settings (15).

In extreme cases, extracorporeal membrane oxygenation

(ECMO) or operative cardiopulmonary bypass has been used to resuscitate unresponsive patients. ECMO can be considered early in cases where traditional resuscitative measures are ineffective to prevent irreversible ischemic acidosis (15).

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