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Clinical Perspective

Epinephrine use for anaphylaxis: Too seldom, too late

Current practices and guidelines in health care

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Clinical Problem

During the past 20 years, food allergy has dramatically increased, with a concomitant increased risk for anaphylaxis.¹ Anaphylaxis is “a serious allergic reaction that is rapid in onset and may cause death.”² Foods are one of the common causes of anaphylaxis³ over medications and insect stings, and food allergy has become a worldwide concern. Anaphylaxis is inadequately treated most of the time⁴ because of inconsistent signs and symptoms; anaphylaxis can manifest differently in the same person, even when triggered by the same allergen. The first emergency medication indicated in anaphylaxis treatment is intramuscular epinephrine.² The most common cause of death from food allergies is delayed epinephrine administration.⁵ This suggests the urgent need to educate health care providers on anaphylaxis diagnosis and appropriate epinephrine use. Guidelines need to highlight appropriate and timely therapy with a focus on epinephrine use as first-line treatment.

Strategies and Evidence

There are no contradictions to the use of epinephrine for a life-threatening allergic reaction.⁶ Epinephrine is so crucial that administration is recommended even with the suspicion of a food allergic reaction occurring.¹ Fatalities occur when epinephrine use is delayed or omitted altogether.⁷

It is difficult to identify anaphylaxis when patients present to emergency departments (EDs) feeling better by the time they arrive. This happens when the body naturally secretes adrenalin owing to stress or when patients use antihistamines to treat cutaneous symptoms. Although antihistamines help cutaneous symptoms, they do not alleviate respiratory distress or shock.⁸ Another

common and incorrect treatment occurs when health care providers far too often treat patients with diphenhydramine in the ED.² Cutaneous symptoms, including erythema, urticaria, pruritus, and angioedema, are common and typically treated with antihistamines. It is important to continue to closely monitor these patients to ensure that other anaphylactic symptoms do not manifest. The delayed or partial administration of epinephrine owing to improper technique increases the risk for a second reaction.⁵

Patients with anaphylactic reactions are often discharged from EDs without a prescription for an epinephrine auto-injector (EAI), education, or referral to a specialist.⁹ Health care providers, who are the first line of contact with patients, need to educate patients on the importance of an EAI and demonstrate proper technique using a training device.¹ This needs to be followed up by the patient's personal care team to remind and enforce the carrying of an EAI at all times.

Areas of Uncertainty

Current Practices

Anaphylaxis mismanagement can be fatal. Multiple worldwide studies have illustrated inconsistent management of anaphylaxis despite recommendations provided in guidelines.² A study of the UK registry reported that nearly 40% of all anaphylactic deaths did not receive any epinephrine.¹⁰ Song et al² reported similar results from a 2-month US study of 34 hospitals where 2,333 ED visits for anaphylaxis occurred with only 19% of patients receiving epinephrine. Another study reviewing 2,114 patients from Germany, Austria, and Switzerland who presented with severe anaphylaxis discovered that fewer than 14% were treated with epinephrine.² Clark et al⁹ summarized emergency visits for 678 anaphylactic reactions and identified 50% as severe. Of these cases, 90% received antihistamines, 50% received systemic steroids, and only 16% received epinephrine. Further investigation at discharge showed only 40% mentioned allergen avoidance, 16% prescribed epinephrine, 12% referred to an allergist, and only 2% of patients received all 3 interventions.⁹

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A study of Canadian children from 2004 through 2009 with physician-confirmed peanut allergy showed that severe reactions were treated with epinephrine only 21% of the time.¹¹ Sicherer and Simons¹ identified 13 children who experienced anaphylaxis to food, and 6 episodes were fatal owing to delayed epinephrine administration. The 7 children who survived were given epinephrine within the first 5 minutes of the reaction. This study emphasizes the importance of prompt epinephrine administration. A study in Australia that explored fatal anaphylaxis to foods categorized a delay in epinephrine as any period longer than 20 minutes.¹²

The available evidence shows that anaphylactic reactions are often treated with antihistamines, bronchodilators, and prednisone,¹¹ but using them as first-line treatments, thus delaying timely epinephrine administration, in cases of suspected anaphylaxis is inappropriate. Paramedics are first responders with emergency medical services. Discussions with emergency pharmacist T. Furst in a Canadian pediatric hospital in 2013 showed that, at times, paramedics administer epinephrine in the arm rather than the leg. Although administration can be subcutaneous or intramuscular in the deltoid or vastus lateralis, the vastus lateralis has the fastest absorption rate.² Patient morbidity and health care costs are being affected by the variable use of epinephrine by health care providers.¹³ Health care providers, spanning from ED physicians, nurses, and paramedics to family physicians, pediatricians, allergy educators, and school nurses, need to be properly educated regarding guidelines. A unified voice is crucial to ensure that patients with food allergies receive proper care.

Barriers to Implementation

The World Allergy Organization surveyed allergy and immunology specialists from 44 countries and found 36% used guidelines developed within the country of practice, 34% adopted guidelines from other countries, and 30% did not have any anaphylaxis guidelines.¹⁴ Without any guidelines, health care providers do not have a structured reference to follow. "The importance of having a management protocol cannot be over-emphasized because retention of memorized facts and algorithms can be poor in a crisis and there is little or no time to look up information."⁸

There are several barriers to anaphylaxis treatment. Lack of knowledge of obvious signs, symptoms, and management of anaphylaxis are part of the issue, in addition to a lack of understanding of the evidence associated with it. One study found that a delay in epinephrine treatment for children resulted from a lack of ability to recognize anaphylactic symptoms and was compounded by not following emergency guidelines.¹⁵ One case study described an anaphylactic reaction that resulted in a fatality when the physician misdiagnosed the patient as having an anxiety attack.⁷ Because this type of severe allergic reaction occurs in only approximately 2% of the population,¹⁶ the knowledge deficit can be attributed to the lack of firsthand experience of the health care provider.

The European Academy of Allergy and Clinical Immunology has publically announced that all individuals diagnosed with a food allergy must carry an EAI.² Song et al² described many challenges associated with carrying an EAI, such as the lack of availability in some countries, prohibitive costs to obtaining an EAI, not carrying the device, and improper use.²

In urban settings, patients tend to rely on emergency medical services rather than self-treatment.¹⁷ Although there can be several reasons for or barriers to using epinephrine on oneself when experiencing anaphylaxis, a health care provider using antihistamines for anaphylaxis rather than epinephrine in an emergency setting unintentionally demonstrates that epinephrine is not necessary to treat anaphylaxis. This creates a false sense of "appropriate management" in patients' minds. For the proper

message to be translated to the public, it must be practiced by those who preach it. For instance, it is not uncommon for parents to be aware of the need for epinephrine, yet during their child's anaphylactic reaction, they fail to administer the auto-injector, possibly because of fear of using a needle⁴ and physically hurting their child. Instead, they take a risk by driving their child to the ED rather than calling an ambulance, and the child is not treated with epinephrine. The child survives, reinforcing the idea that the treatment provided by the health care providers was correct, their actions were appropriate, and epinephrine was not required. Because most cases of inappropriately treated anaphylaxis do not end in fatalities, this scenario is continually repeated, reinforcing inadequate treatment and increasing the risk of morbidity and fatality. The benefit for patients to carry and use an auto-injector is lost on them when they see health care providers in an emergency situation not using epinephrine promptly.

Implementation Strategies

Recently, more emphasis has been placed on knowledge translation. Although there are discussions about the benefits of adapting guidelines to fit a specific organization, anaphylaxis treatments are specific and not dependent on special equipment or personnel. Strategies can include interactive educational sessions directed toward health care providers and initiation of specific care maps. Because passive learning is inadequate, it is important to apply new knowledge at the time of decision making.¹⁸ After an anaphylactic admission, discussions or case scenarios can be presented at staff meetings to highlight appropriate guideline use and generate discussions that allow ongoing education for health care providers at the organization. One study in the United States implemented an electronic guideline on a local network, including an order set for anaphylaxis management, and assessed whether diagnosis and management changed after implementation. After implementation of guidelines, there were more anaphylaxis diagnoses, possibly because of the education, more hospital epinephrine administration, and a decrease of hospital admission.¹⁹ This reinforces the idea that implementation strategies work if they fit within the organizational structure.

Visual aids, such as posters or a care map, can be a helpful reminder. Visualizing a schematic diagram can provide a stepwise, structured approach to managing a possibly confusing situation. This timely implementation not only will be conducive to reinforce practice but also can be a learning opportunity for health care providers to recognize the multiple facets of anaphylaxis. Feedback can be instrumental when implementing change; therefore, review and discussion of case management might help to teach and reinforce staff.

Management of food allergy requires specific knowledge about allergen avoidance, reading food labels, recognizing symptoms of a reaction, and using an EAI.²⁰ There is a need for more non-allergist health care providers to be educated on the topic of food allergies to meet the medical needs of their patients so that they are prepared and confident in their ability to manage a reaction.²⁰

Guidelines

Experts in allergy and clinical immunology around the world unanimously agree that prompt administration of epinephrine is the first line of anaphylaxis treatment.² Guidelines from the American Academy of Allergy, Asthma & Immunology and the American College of Allergy, Asthma & Immunology recommend prompt epinephrine administration at the first indication of anaphylaxis and even go as far as to suggest administering the medication when in doubt.² Currently, there are only 2 preset doses of EAI's available in North America. For any individual weighing more than 25 kg, the recommended intramuscular epinephrine

dose is 0.3 mg. A patient weighing 10 to 25 kg should receive 0.15 mg of epinephrine. For children weighing less than 10 kg, epinephrine dosing becomes more complex. With a recommended dose of 0.01 mg/kg, there is potential for overdosing when using prefilled EAls.¹ However, given the option of epinephrine ampules and a syringe, until lower-dose EAls are available, the 0.15-mg EAls are preferable.

Conclusions and Recommendations

Morbidity and mortality from anaphylaxis are associated with delay or lack of epinephrine use. This risk can be minimized by recognizing the variable signs and symptoms of anaphylaxis and treating promptly with intramuscular epinephrine. Reviewing guidelines and implementing strategies that enforce epinephrine as the first line of treatment could be helpful. It is imperative that hospitals, clinics, and other health care organizations emphasize appropriate use of epinephrine for best patient outcome, consistency of care, and health promotion within the community. Health care providers, spanning from ED physicians, nurses, and paramedics to family physicians, pediatricians, allergy educators, and school nurses, need to be properly educated regarding guidelines. Strategies should focus on improving education of health care providers who deal with anaphylactic reactions.

In addition to immediate health benefits to individuals living with a food allergy, using an anaphylaxis guideline will significantly lower costs to EDs and intensive care units as the number of severe reactions decreases over time. Using a framework or model to guide implementation can help incorporate guidelines effectively and evaluate their adoption. Strategies should focus on improving education of health care providers who treat patients with food allergy and anaphylactic reactions as a first step (but not the only step). By ensuring that the standard of care adheres to the best available evidence, the outcomes of anaphylactic reactions can be improved for patients, health care providers, and the organizations involved.

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