10.58931/cait.2024.4375

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At-home Management of Food-induced Anaphylaxis

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Introduction: Anaphylaxis

Anaphylaxis is an acute, potentially life-threatening, systemic reaction characterized by the involvement of two or more body systems.[1] The National Institute of Allergy and Infectious Diseases and Food Allergy and Anaphylaxis Network (NIAID/FAAN) have well-established criteria for the clinical definition of anaphylaxis.[2] Anaphylaxis is a severe allergic reaction that occurs suddenly after contact with an allergy-causing substance (e.g., peanuts), insect venom or medications (e.g., antibiotics). Anaphylaxis criteria include an acute onset of symptoms (within minutes to several hours) involving the skin, mucosal tissue, or both, which may present with generalized hives, pruritus or flushing, or swollen lips, tongue, and uvula. In addition, one or more of the following must be present: respiratory compromise, reduced blood pressure, or associated symptoms of end-organ dysfunction. Anaphylaxis results in a sudden release of mediators, including, but not limited to, histamine from activated mast cells and basophils following the cross-linking of specific immunoglobulin E. Together with downstream mediators, such as prostaglandin D2, platelet activating factor, and leukotrienes, this reaction manifests clinically through peripheral vasodilation, bronchoconstriction, and increased vascular permeability, presenting as a multi-organ emergency requiring immediate intervention.[3]

It is estimated that up to 5% of the population has experienced anaphylaxis, although fatality rates are very low at approximately 0.3% and occur most commonly with drug-induced anaphylaxis.[4,5] Older age, often consistent with pre-existing comorbidities, and delayed epinephrine administration, pose the most significant risk factors for anaphylaxis fatality. While the global rates of anaphylaxis appear to be on the rise, case fatalities fortunately do not seem to follow this trend.[6]

Anaphylaxis is uniphasic in the majority of cases, whereby symptoms peak within 60 minutes and resolve within the next hour without any symptom recurrence.[7] Less commonly, anaphylaxis may be persistent (symptoms lasting for at least 4 hours), refractory (the initial reaction is treated with 3 or more doses of epinephrine in addition to other management strategies and remains unresolved), or biphasic (symptoms recur between 1 and 48 hours following the complete

resolution of the initial reaction.[8] Biphasic reactions are estimated to occur in between 4% and 20% of cases and are often associated with initial reactions of greater severity.[9-12]

Epinephrine in Anaphylaxis Management

The role of epinephrine in the management paradigm for anaphylaxis cannot be over-emphasized – it is essential first-line treatment. In addition to being fast-acting, it is the only treatment that stabilizes mast cell membranes halting the release of more mediators and can reverse the life-threatening respiratory and cardiac symptoms.[13,14] The timely administration of epinephrine is paramount to the reduction of anaphylaxis mortality and morbidity, including biphasic reactions.[15] There are no substitutes or contraindications for the use of epinephrine. Recent evidence updates support the repeated administration of intramuscular epinephrine if symptoms do not improve within 5 minutes of the previous dose.[16]

Autoinjectors administer epinephrine intramuscularly usually into the anterior lateral thigh, with a recommended dosage based on weight. This is the fastest route of administration, achieving a peak plasma epinephrine concentration in 6 to 10 minutes, compared to subcutaneous administration, which may take 20 to 48 minutes.[13] More recently, a novel intranasal epinephrine preparation was found to be safe, well-tolerated and fast-acting (median time to peak plasma concentration was 2.5 minutes).[17] This needle-free design has received approval from the European Union's European Medicines Agency and the United States Food and Drug Administration.[18,19]

Adjunct symptom management therapies, including intravenous bolus, supplemental oxygen and beta-2 agonists, may be considered following stabilization with epinephrine to mediate hypotension and persisting respiratory symptoms. The use of antihistamines in the management paradigm is limited to providing relief for persisting cutaneous symptoms.[16]

Shifting the Paradigm of Anaphylaxis Management

In some situations, it may be appropriate to manage food-induced anaphylaxis at home using epinephrine without having to call emergency medical services (EMS). In 2020, during the COVID-19 pandemic, Casale et al published an updated anaphylaxis management algorithm intended to reduce the burden on healthcare services and lower the risk of infection. The revised algorithm included the important note that for severe cases of anaphylaxis, the usual procedure of immediately contacting EMS after using epinephrine should still be adhered to.[20] In 2022, Casale et al published a follow-up article examining the possibility of managing anaphylactic events at home, even outside of a pandemic. The authors argued that with proper selection, education and access to the right medications, patients can safely manage an anaphylactic event using a home management algorithm. Furthermore, they argued that this approach should reduce the need for a hospital Emergency Department (ED) visit and is likely to improve outcomes due to quicker administration of epinephrine.[21]

Following this, a notable shift occurred in the field, prompting widespread debate and reassessment of this long-established algorithm for anaphylaxis management **(Figure 1)**. In 2023, Dribin et al published an article in *Journal of Allergy and Clinical Immunology: In Practice* discussing the epinephrine auto-injector prescription; use for optimal clinical care of individuals at risk of anaphylaxis; proposing an alternative treatment algorithm.[22] Greenhawt et al also advocated retiring routine EMS activation after epinephrine use in their perspective article in *Annals of Allergy, Asthma and Immunology*.[23] The Canadian Society of Allergy and Clinical Immunology (CSACI) published their considerations for at-home management of food-induced anaphylaxis.[24] The rationale for implementing the updated guidance for home management has been discussed at length in each of these articles and is summarized in **Table 1.** In considering this guidance, at-home anaphylaxis management could occur under certain circumstances that begin with the patient and caregiver's comfort level and preference, access to at least two in-date, weight-appropriate doses of epinephrine autoinjectors, absence of risk factors for a biphasic reaction or severe anaphylaxis outcomes,[26-28] and symptoms resolution with one dose of epinephrine administration.[24] However, at-home management of anaphylaxis may not be appropriate under certain considerations, as outlined in **Table 2.**[25]

This proposed algorithm has challenges. Many patients don't carry more than one dose of epinephrine; reports show that fewer than half of people always have more than one epinephrine

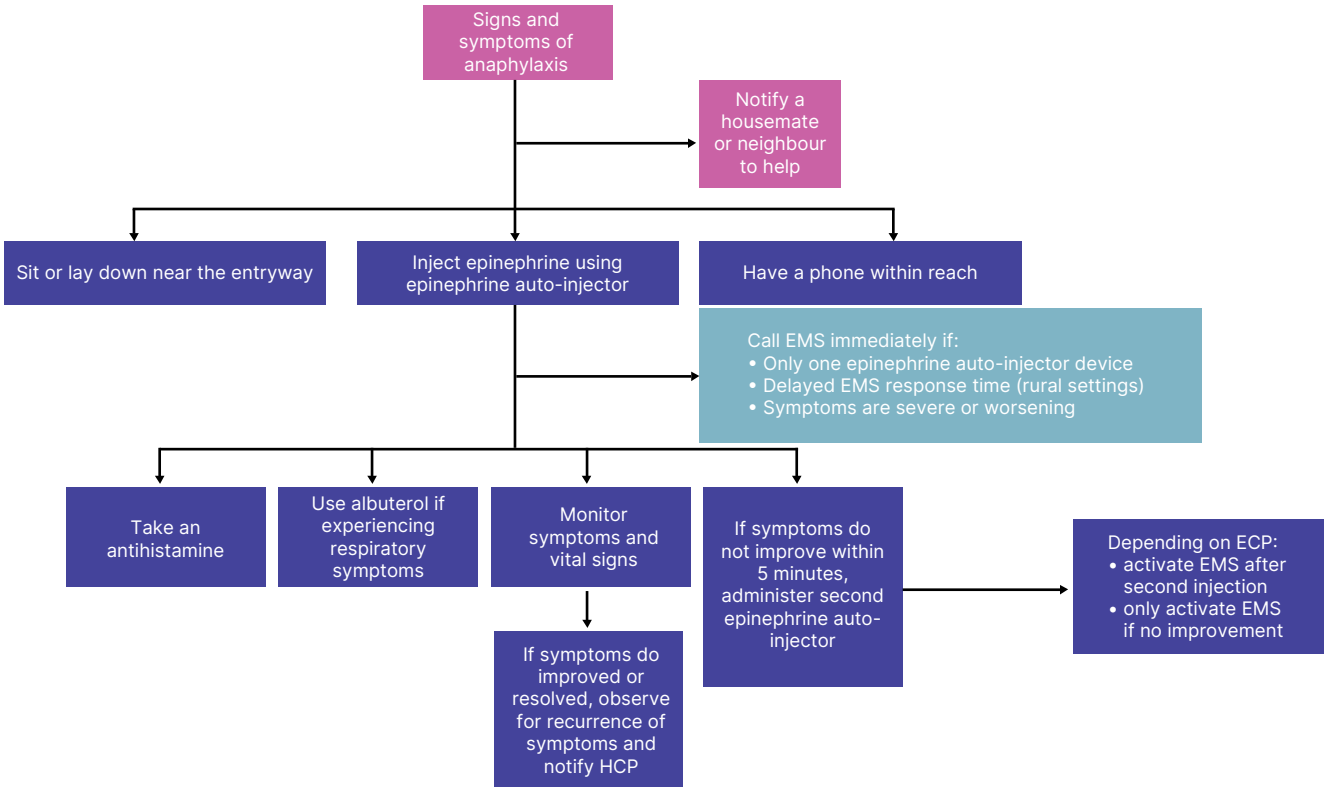

Figure 1. Proposed algorithm for at-home management of food-induced anaphylaxis. Adapted from Casale et al and Dibrin et al.
Abbreviations: EMS: Emergency medical services; **ECP:** Emergency care plan

1. Requiring EMS activation might lead to associating the use of epinephrine with needing EMS, which could result in delaying or avoiding the use of intramuscular epinephrine.
2. Fatalities from anaphylaxis are extremely rare.
3. Severe biphasic anaphylaxis and deaths from biphasic anaphylaxis are extremely rare.
4. Early administration of epinephrine is the most effective way to prevent biphasic and other severe anaphylaxis reactions, including those requiring intensive care unit or hospital admission.
5. Intramuscular epinephrine is very safe and does not require monitoring in the hospital ED; it can be managed safely at home.
6. Additional treatments given in the ED, like antihistamines and corticosteroids, have not been shown to reduce the risk of biphasic reactions or fatalities.
7. Routine EMS activation for anaphylaxis that has resolved after epinephrine treatment is not very beneficial and incurs high healthcare costs ($142 million per life-year saved and $1.4 billion to prevent one death).
8. There are significant issues with healthcare resource use in hospital EDs and increased risks of infection transmission, including COVID-19 and other respiratory viruses.

Table 1. Rationale for at-home management of anaphylaxis with epinephrine use.[20-25]

1. Patient and caregiver are not comfortable with managing anaphylaxis without contacting EMS or visiting the ED.
2. Epinephrine autoinjectors are not available or only one autoinjector is available.
3. Being alone, without immediate access to a caregiver for assistance if needed.
4. Being unaware of the allergic symptoms that necessitate using an epinephrine autoinjector.
5. Lack of technical skills for using an epinephrine autoinjector.
6. Hesitancy about the intramuscular injection due to needle phobia.

Table 2. Factors to consider against managing anaphylaxis at home.[25]
Abbreviations: EMS: Emergency medical services; **ED:** Emergency department

auto-injector on hand.[29] Additionally, some patients and caregivers may not know how to use epinephrine or monitor symptoms properly. Assessing whether patients or caregivers are "capable and compliant" is often subjective and can be influenced by personal biases.[22]

Importantly, these discussions have highlighted gaps in our understanding of anaphylaxis treatment. Variations in the use of epinephrine may arise from inconsistencies in how anaphylaxis is defined. One of the most significant evidence gaps in allergy care is our inability to predict the risk of severe future reactions or biphasic reactions.[30] While our understanding of the risk factors and co-factors that may worsen reactions is improving, further research is needed to determine if emergency care plans enhance anaphylaxis care and outcomes.[31] Additionally, research should focus on improving these plans to better address the needs of patients and caregivers. Reliable strategies are necessary to assess how well patients and caregivers can recognize and manage reactions and enhance their performance through targeted educational interventions.[22] In conclusion, until an algorithm for home management can be verified to be safe and effective, it will face barriers to widespread adoption by relevant stakeholders.

Summary

Anaphylaxis is a severe, potentially life-threatening allergic reaction involving multiple organ systems, typically triggered by foods, insect stings, or medications. It results from rapidly releasing histamine and other inflammatory mediators, leading to peripheral vasodilation and bronchoconstriction, among other manifestations. Prompt administration of epinephrine is crucial, as it is the only treatment that effectively counteracts these severe reactions. The management of anaphylaxis, particularly at home, has been evolving. Recent discussions suggest that some cases could be managed at home with proper education and resources to reduce hospital ED visits, and hopefully encourage epinephrine auto-injector use given reluctance to present to the ED. However, this approach faces challenges such as ensuring patients have multiple doses of epinephrine on hand and are appropriately trained. There is a call for further research to refine treatment guidelines for at-home management of anaphylaxis, and to improve patient outcomes.

The author wishes to acknowledge the help of Lubnaa Hossenbaccus, MSc and Sophia Linton, BSc in preparing this manuscript.

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Financial Disclosures

A.K.E.: Advisory boards: AstraZeneca, Bausch Health, GSK, Miravo, Merck, Novartis; **Speaker:** ALK Abello, AstraZeneca, Bausch, Miravo, Medexus, Novartis, Pfizer, Sanofi, StallergenesGreer and Regeneron. **Institutional grant funding:** ALK Abello, Aralez, AstraZeneca, Bayer LLC, Medexus, Novartis, Sanofi and Regeneron. **Independent consultancy:** Bayer LLC, Pharming, and Regeneron.

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