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Physician Instructions to Inject Epinephrine with Mild or No Symptoms on Food Allergy and Anaphylaxis Emergency Plans.

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Conflicts/Declarations

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Clinical Implication: Wide variations in physicians advising epinephrine for no/mild symptoms on anaphylaxis plans suggests more research and education is needed on making these decisions.

To the Editor:

Anaphylaxis is a potentially life threatening allergic reaction that requires prompt medical treatment with epinephrine.(1-4) In 2004, the National Institute of Allergy and Infectious Diseases and the Food Allergy and Anaphylaxis Network defined anaphylaxis “as a serious allergic reaction that is rapid in onset and may cause death.”(1) Food is the most common trigger causing anaphylaxis in the community setting. Patients at risk of life-threatening food-allergic reactions must have prompt access to an epinephrine autoinjector (EAI) and understand when and how to use it. An important component of preparation is providing and reviewing a written emergency plan to help patients and caretakers assess symptoms and provide appropriate treatment. (2, 3)

Of note, some plans, including those from the Food Allergy Research and Education (FARE) and American Academy of Pediatrics (AAP), provide the option for the prescriber to list allergens the patient is severely allergic to, with instructions to administer epinephrine even if the patient has mild symptoms or no symptoms. These options are controversial.(3, 5, 6) The reasoning behind these recommendations primarily developed from an early report from the American Academy of Allergy, Asthma and Immunology that in the event of a history of extremely severe past reactions, and a known ingestion, it may be reasonable to treat immediately with no or mild symptoms because symptoms will be expected and epinephrine may prevent the reaction from escalating.(7) However, this approach has never been studied and there are concerns that early use of the EAI may be ineffective if the epinephrine plasma levels

peak prior to the most severe symptoms.(5, 6) Additionally, epinephrine injections have some unpleasant side effects. Despite the potential negatives, the instruction to give EAI after ingestion of the allergen, even if there are mild or no symptoms, may help lessen the chance of delay in injection or confusion in assessing symptoms during first aid management.(6-8) Additionally, this recommendation may be beneficial for patients with past severe anaphylactic reactions or have asthma, the strongest associated comorbidity with anaphylaxis. (7, 9)

In this descriptive study, we sought to evaluate how often allergists and pediatricians use these controversial options and the clinical reasoning behind those decisions. We conducted a physician survey and also a separate retrospective chart review. Surveys were administered to a convenience sample of allergists and pediatricians both via email and in-person to multiple physicians in practice settings in Manhattan, New York. Email addresses were attained via an internet search of allergists and pediatricians on the Mount Sinai website and three rounds of emails were sent to 168 practitioners. Local allergists and pediatricians were also located via an internet search and surveys were physically delivered to the office. Surveys were anonymous and asked the respondent to approximate their frequency (i.e., “Never”, “1-9%”, “10-19%”, etc. on through “100%/always”) of indicating on the plans to inject epinephrine for ingestions with mild symptoms (Option A) and indicating to inject epinephrine for ingestions without symptoms (Option B) as shown in **Figure e1** (survey), along with their reasons for selecting the options. The surveys included examples of the Options (See **Figure e1**). A separate retrospective chart review of 1,000 food allergy action plans in the referral practice of the Jaffe Food Allergy Institute was performed and information regarding practitioner, patient age, food allergy type, past reaction history, and medical comorbidities was obtained. The charts of 9 pediatric allergists

were included in the chart review. Comparisons were made via chi-square analyses. The studies were approved by the Mount Sinai Program for the Protection of Human Subjects.

Overall, the survey response rate was 35.4% (69/195) and 58 respondents reported having written an action plan (15 allergists, 43 pediatricians), as shown in **Figure e2**, consort diagram. Respondents who did not write a food allergy action plan were excluded. Overall, 100% of the allergists (n=15) and 74% (32/43) of the pediatricians were familiar with the choice to inject for mild symptoms (“Option A”); 93% and 72% for injecting upon ingestions with no symptoms (“Option B”), respectively. Allergists (80%) indicated that they used Option A in 1-9% of plans, compared to 28% of pediatricians ($p<.05$). Most allergists (57%) used Option B in 1-9% of plans, compared to 26% of pediatricians ($p=.05$). In addition, 20% of allergists and 44% of pediatricians used Option A ($p=.11$) in over 9% of plans; 14% of allergists and 40% of pediatricians used Option B ($p=0.09$) in over 9% of plans (**Figure 1**). Most common reasons to use the options for both allergists and pediatricians included past anaphylaxis, pediatric intensive care unit (PICU) admission, intubation, and cardiovascular collapse. PICU admission ($p=0.03$), intubation ($p=0.01$), and cardiovascular collapse ($p=0.002$) were identified more often as driving factors by allergists as compared to pediatricians (**Figure 2**). In the chart review, overall option usage was 4.1% and when analyzed by provider, usage rates varied from 0-9%, depending on the provider. Thus, the observed option use by the allergists was consistent with the survey where the majority of allergists (not the same group) indicated using the options in the 0-9% range. Options were used more often in cases where the patient had any asthma ($p<0.001$), mild intermittent asthma ($p<0.01$), mild persistent asthma ($p<0.01$), moderate persistent/severe asthma ($p<0.05$), any asthma treatments ($p<0.001$), acute asthma medications ($p<0.01$), controller asthma medications ($p<0.001$), past anaphylaxis ($p<0.001$), or past epinephrine use ($p<0.001$).

In summary, we found that use of these options by physicians varied widely, from being never used to being used for every patient. It appears that conceptually the options are being used as proposed since past severe reactions and risk factors associated with anaphylaxis are a driving force for option usage. However, the wide range of option usage (28% of the physicians “always” or “never” used Option A [43% for Option B]) and lack of awareness about the options from pediatricians suggests that further education on the usage of the options is needed. The limitations of this study include a low participation rate (although higher than typical for physician surveys) and the use of a regional convenience sample that may introduce bias and limit generalizability. Furthermore, we do not truly know the value of selecting these options and outcomes research on the clinical ramifications are needed to develop evidence-based guidelines.

Bibliography

1. Sampson HA, Munoz-Furlong A, Campbell RL, Adkinson NF, Jr., Bock SA, Branum A, et al. Second symposium on the definition and management of anaphylaxis: summary report--Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol* 2006;117(2):391-7.
2. Boyce JA, Assa'ad A, Burks AW, Jones SM, Sampson HA, Wood RA, et al. Guidelines for the Diagnosis and Management of Food Allergy in the United States: Summary of the NIAID-Sponsored Expert Panel Report. *J Allergy Clin Immunol* 2010;126(6):1105-18.
3. Mercer RD, Jones CJ, Smith HE. Reviewing the Content and Design of Anaphylaxis Management Plans Published in English. *J Allergy Clin Immunol Pract*. 2017;5(5):1288-94.
4. Pumphrey RS. Lessons for management of anaphylaxis from a study of fatal reactions. *Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology*. 2000;30(8):1144-50.
5. Turner PJ, DunnGalvin A, Hourihane JO. The Emperor Has No Symptoms: The Risks of a Blanket Approach to Using Epinephrine Autoinjectors for All Allergic Reactions. *J Allergy Clin Immunol Pract* 2016;4(6):1143-6.
6. Wang J, Sicherer SH. Guidance on Completing a Written Allergy and Anaphylaxis Emergency Plan. *Pediatrics*. 2017;139(3).
7. American Academy of Allergy AaI. Anaphylaxis in schools and other childcare settings. AAAAI Board of Directors. American Academy of Allergy, Asthma and Immunology. *J Allergy Clin Immunol*. 1998;102(2):173-6.
8. Sicherer SH, Simons FE, Section on A, Immunology AAoP. Self-injectable epinephrine for first-aid management of anaphylaxis. *Pediatrics*. 2007;119(3):638-46.

- 133 9. Burks AW, Jones SM, Boyce JA, Sicherer SH, Wood RA, Assa'ad A, et al. NIAID-
134 sponsored 2010 guidelines for managing food allergy: applications in the pediatric population.
135 Pediatrics. 2011;128(5):955-65.

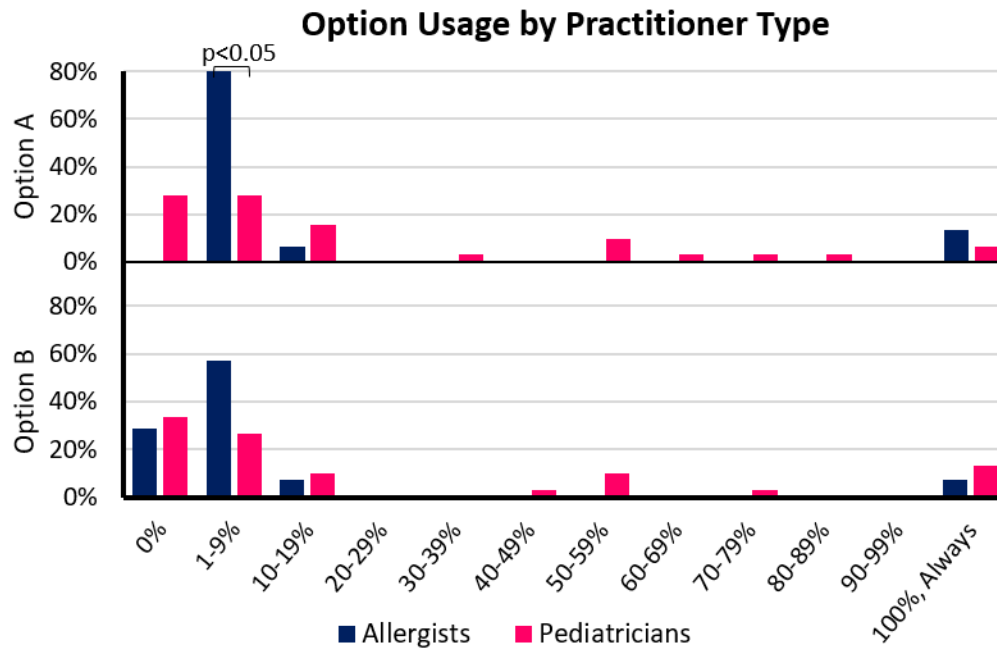
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138 Figure 1. Allergists (80%) used Option A in 1-9% of plans, compared to 28% of pediatricians
139 ($p<.05$). Allergists (57%) used Option B in 1-9% of plans, compared to 26% of pediatricians
140 ($p=.05$).

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142 Figure 2. Reasons to use the options varies by practitioner type. Top reasons to use the options
143 for both allergists and pediatricians included past anaphylaxis, PICU admission, intubation, and
144 cardiovascular collapse and these were identified more often by allergists ($p<0.05$).



Reasons to Use Option A or Option B

