Assessing Anaphylaxis: Improving Residents' Identification of a Life-Threatening Condition via a Focused Didactic and Case-Based Discussion

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ABSTRACT

INTRODUCTION: Anaphylaxis is a life-threatening condition encountered by all physicians and healthcare providers. Data indicate that physicians often fail to recognize this syndrome, leading to misdiagnosis, mismanagement, and adverse outcomes. This educational program aimed to assess knowledge about anaphylaxis in a cohort of internal medicine residents and develop and test the efficacy of an educational intervention in addressing gaps in understanding of this critical condition.

METHODS: An in-person educational intervention, including a lecture and case-based open discussion, was delivered to 44 internal medicine residents at an academic medical center with pre- and post-intervention self-assessments. Our primary outcome was the change in the rate of residents being able to correctly identify critical features of anaphylaxis and appropriate treatment. Longer-term follow-up was completed in a subset of residents to assess knowledge retention.

RESULTS: Immediately following the educational intervention, there was increased likelihood of diagnosing anaphylaxis in a written case scenario from 69% to 91% (RR: 1.30; 95% CI 1.09,1.56) and reporting the correct dose and route of administration of epinephrine from 19% to 95% (RR:4.96; 95% CI: 2.26, 10.88). Residents also demonstrated increased identification of cardiovascular compromise in anaphylaxis, as well as often underrecognized gastrointestinal and neurological symptoms after the intervention. In an assessment evaluating longitudinal retention up to 15 months after the intervention, approximately 50% of those who responded to the longitudinal survey correctly recalled the dosing and route of administration of epinephrine for treating anaphylaxis.

DISCUSSION: A brief educational session on anaphylaxis was successful in improving residents' short-term knowledge about diagnosis and treatment of anaphylaxis and may also impact long-term retention.

KEYWORDS: anaphylaxis; graduate medical education; epinephrine; physicians; diagnostic errors

INTRODUCTION

Anaphylaxis is a life-threatening, systemic physiologic reaction that occurs after exposure to an allergen or trigger. Approximately 5–7% of adults in the United States have experienced a probable anaphylactic reaction,[1] and 1% of hospitalizations and 0.1% of emergency department visits for anaphylaxis are fatal.[2] Among hospitalized patients, anaphylaxis has an incidence of approximately 1.5 events per 5,000 admissions, the majority of which are attributed to medication exposures.[3]

Despite its potentially lethal consequences, anaphylaxis is often underdiagnosed, which can lead to delays in treatment[4,5] and adverse outcomes. Diagnostic delays and misdiagnoses are due to the protean nature of anaphylaxis, which involves a constellation of symptoms encompassing different organ systems. Often these symptoms are not synthesized into a unifying diagnosis of anaphylaxis, but rather are mislabeled as dehydration, "toxic drug effect," or simple urticaria.[6,7] In one emergency department study, 57% of patient visits retrospectively identified as "likely cases of anaphylaxis" did not receive the diagnosis.[8] Other studies have shown that anaphylaxis is missed in up to 80% of patients who are seen in emergency departments, undergo surgical procedures, or are treated with chemotherapy or biological agents.[7]

One potentially harmful consequence of underdiagnosing anaphylaxis as an allergic or hypersensitivity reaction is withholding lifesaving treatment with epinephrine.[9] In cases of anaphylaxis, cardiac or respiratory arrest can ensue within a median time of 5–30 minutes and in one study, with approximately half of fatalities occurring within one hour of symptom onset.[10] Moreover, studies show that physicians favor administration of "safer" agents, such as glucocorticoids and antihistamines, to treat symptoms consistent with anaphylaxis instead of epinephrine, which is considered first-line treatment.[4,9,11] While it is challenging to predict which patients presenting with a systemic allergic reaction will progress to anaphylaxis, epinephrine should be given to anyone at risk.[12] Delayed administration of epinephrine is associated with poor outcomes including hypoxia, tissue ischemia, encephalopathy and death.[9]

Given the life-threatening nature of anaphylaxis, it is important to impart a high degree of clinical suspicion and improve overall knowledge among clinicians, particularly

at the trainee level. Even attending physicians are generally unfamiliar with the management of anaphylaxis and the details surrounding treatment, such as the dosing of epinephrine.[13,14]

There is limited graduate medical education on allergy and immunology as a field and in particular, on the topic of anaphylaxis.[15] Medical residents may not readily encounter a clearly diagnosed case of anaphylaxis and therefore may be unfamiliar with its diagnosis and management.[4,16] Mismanaged cases of anaphylaxis can lead to potentially lethal adverse events that require intensive care unit admissions; for example, administering epinephrine intravenously instead of by intramuscular route is associated with increased risk of cardiovascular adverse events such as arrhythmia or myocardial ischemia.[17,18] It is vital to recognize early symptoms of anaphylaxis and understand when it is appropriate to initiate treatment.

Given this knowledge gap and need for effective curricular materials about this rare and potentially fatal condition, a case-based educational program was developed by the study authors, with multidisciplinary expertise in managing anaphylaxis. Didactic and interactive case-centered methods were utilized as these techniques have been shown to be effective in graduate medical education.[19] A case-based program affords real-life examples and provides concrete structure for those in training with limited clinical experience.[20] In addition, our study captured both quantitative and qualitative data to provide a holistic understanding of residents' knowledge of anaphylaxis. Previously published literature on education regarding anaphylaxis have focused on pediatric anaphylaxis. Our intervention focuses on identifying anaphylaxis in the adult population, and is targeted towards teaching medical residents across adult specialties working in the emergency room, inpatient, and intensive care medical settings.

METHODS

Study Setting and Participants

This study was approved by the Lifespan/Rhode Island Hospital Institutional Review Board (Protocol ID# 1412799). Participants were recruited from a pool of over 120 Brown University Internal Medicine residents. An educational seminar was given during regularly scheduled conference time for residents on inpatient rotations. These sessions took place monthly over a six-month time period, and were typically attended by between five and 15 residents, including PGY-1, PGY-2, PGY-3, and PGY-4 (chief) residents. A total of 44 residents participated in the pre- and post-testing with a response rate of over 90% of attendees.

Intervention

The intervention was delivered in-person using a slideshow presentation for eight sessions. The module (**Appendix A**) was delivered to peers, by first author (HM) who was a senior resident during the time of the study. The content was curated from background research, guidelines from the National Institute of Allergy and Infectious Diseases, patient cases, and input from the pulmonary, critical care and sleep medicine and allergy and immunology faculty (KS, DB, RS). Learning objectives included the definition of anaphylaxis, basic pathophysiology (IgE and non-IgE mediated pathways), clinical signs and symptoms, and treatment of anaphylaxis. In addition, mimics of anaphylaxis including angioedema were discussed. The curriculum consisted of a 30-minute lecture followed by case presentations based on real-life patient scenarios.[17] There was an interactive, open-ended discussion on management of each clinical case. Sessions were performed with small groups of five to 11 residents, to enhance resident participation.

Pre-and Post-Curriculum Assessment

Pre- and post-curriculum assessments (**Appendix B**) were administered in-person using paper surveys prior to and immediately following the didactic intervention to assess participants' knowledge regarding anaphylaxis. Both pre- and post-curriculum surveys contained identical content and were matched using an alphanumeric code. Surveys incorporated both open-ended and multiple-choice questions and took about 10 minutes to complete. Open-ended questions were created by HM with guidance from JK, an expert in educational evaluations, to capture residents' original, unbiased perspectives on the definition, features and treatment of anaphylaxis. Testing case series were created by HM and refined by DB and KS. Residents were asked to read case scenarios depicting anaphylaxis, angioedema, and febrile non-hemolytic blood transfusion reaction, and to identify diagnosis and management in these cases. The longitudinal follow-up survey (**Appendix C**) was administered by emailing an online survey link via REDCap[21] to participants who voluntarily provided their contact information for longitudinal data collection.

ANALYSES

We performed qualitative and quantitative analyses of participants' pre- and post-session assessments. To analyze the open-ended survey item asking for the definition of anaphylaxis, each response was assigned between 0-3 points based on whether the participant mentioned the three key aspects of anaphylaxis as defined by the National Institute of Allergy and Infectious Diseases (NIAID),[14,2] i.e., (1) that it is characterized by a global or systemic physiological response; (2) is a response to an allergen or trigger; and (3) involves cardiovascular compromise. We also tallied the number of organ systems (skin, respiratory, cardiovascular, gastrointestinal, neurologic) mentioned in each response. HM and DB scored answers independently and then reviewed discrepancies

and determined a final score. Author KS served as a third reviewer and independently scored each response. Cohen's kappa analysis yielded kappa of 0.89, indicating high degree of agreement between the reviewers.

Quantitative analyses were conducted in Stata version 17.0 (StataCorp LP, College Station, Texas). Counts (percentages) and medians (interquartile range) of examined variables are presented. Generalized estimating equation (GEE) models were used to evaluate the differences between pre- and post-curriculum knowledge. Applying GEE models enabled us to use all available data for each participant regardless of whether or not they participated in both the pre- and post-surveys and to take into account within-participant correlation of data. Risk ratios and 95% confidence intervals were estimated for dichotomous variables by specifying Poisson distribution, log link, and robust standard errors.

RESULTS

Participants

A total of 44 residents participated, with 41 completing both pre- and immediate post-intervention surveys and three completing only the post-intervention survey. Eighteen residents (40.9%) participated in the longitudinal follow-up survey which was administered between <10–15 months following the instructional session (for 16 surveys with available completion timestamp; mean = 235 days, range: 142 days to 460 days). Most participants (41%, n=17) were interns, with 24% (n=10) post-graduate year (PGY)-2, 31% (n=13) PGY-3 and 5% (n=1) PGY-4 residents.

Knowledge about the Definition of Anaphylaxis

Only 21.9% of residents correctly identified all three components of the definition of anaphylaxis in the pre-curriculum assessment (**Table 1**). While most residents (85.4%) could identify that anaphylaxis was a reaction in response to a trigger, only 58.5% indicated a systemic response and only 43.9% reported cardiovascular compromise as part of the definition prior to the intervention. Sample responses on the definition of anaphylaxis preceding the intervention ranged from "extreme allergic reaction" to "histamine-mediated hemodynamic instability with decreased blood pressure and respiratory distress." Some residents identified histamine release or the role of immunoglobulin E (e.g., "IgE overactivation secondary to allergic reaction"); however, most residents provided clinically-based responses. For example, one participant defined anaphylaxis as an "allergic reaction to a trigger resulting in difficulty breathing and possible swelling of the oropharynx with hypotension."

Table 1. Percentage of residents correctly identifying three major components of the definition of anaphylaxis.

Component of Definition Correct	Pre-Curriculum Survey (%)	Post-Curriculum Survey (%)	RR (95% Confidence Interval)[1]
Component: Systemic	58.5	55.8	0.95 (0.67,1.35)
Component: Shock	43.9	60.5	1.39 (0.99,1.96)
Component: Response	85.4	88.4	1.04 (0.89,1.22)
≥1 Component of Definition	97.6	97.7	1.00 (0.93,1.07)
≥2 Components of Definition	68.3	74.4	1.10 (0.87,1.40)
All components of Definition	21.9	32.6	1.52 (0.82,2.81)

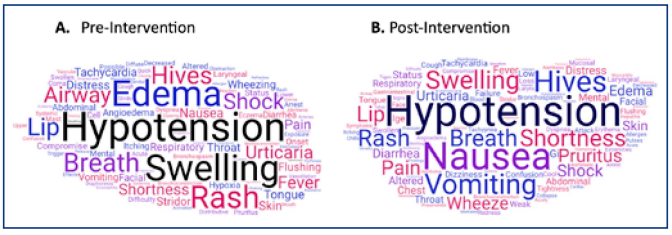
1 Pre vs. post difference estimated with generalized estimating equations specifying Poisson distribution, log link, and robust standard errors

There was marked improvement in residents' ability to identify all three components of the definition correctly immediately following the educational session (32.6% post vs. 21.9% pre; RR 1.52; 95% CI 0.82, 2.81). The greatest improvement was seen in the incorporation of cardiovascular compromise and shock as part of the definition (60.5% post vs. 43.9% pre; RR: 1.39; 95% CI: 0.99,1.96).

Knowledge about the Features of Anaphylaxis

Prior to the intervention, residents could not identify several key features of anaphylaxis across organ systems, except for skin (**Figure 1A,B; Table 2**). Most residents identified dermatological symptoms of anaphylaxis both before and after the intervention; however, immediately following the intervention, residents demonstrated increased reporting of respiratory (RR 1.16; 95% CI 0.90,1.50); cardiovascular (RR 1.12; 95% CI 0.98,1.28); gastrointestinal (RR 4.67; 95% CI 2.21, 9.87), and neurological symptoms (2.25; 95% CI 0.83,6.06) (**Figure 1 A,B; Table 2**).

Figure 1. Pictorial representation of residents' responses, with the relative size of words corresponding to the proportion of residents who cited it.



On the longitudinal follow-up survey, 100% of respondents (n=18) identified dermatological symptoms of anaphylaxis (RR 1.10; 95% CI 1.00, 1.21), vs. 88.9% pre- and 86.7% immediately post-curriculum (RR 0.97; 95% CI 0.85, 1.11). Additionally, 94.4% identified respiratory features (RR 1.34; 95% CI 1.06, 1.69) vs. 68.9% reported pre- and 80.0% immediately post-curriculum (RR 1.16; 95% CI 0.90, 1.50) (**Table 2**). There was, however, a drop in identification of cardiovascular features of anaphylaxis (RR 0.91; 95% CI 0.47, 1.76) in the longitudinal cohort to 70.6% as compared to 75.6% pre- and 84.4% immediately post-curriculum (RR 1.12; 95%

Table 2. Percentage of residents incorporating key organ symptoms involved in anaphylaxis as well as critical aspects of management.

	Pre-Curriculum Survey	Immediate Post-Curriculum Survey		Longitudinal Post Curriculum Survey	
	Col. %	Col. %	RR (95% Confidence Interval)[2]	Col. %	RR (95% Confidence Interval)[3]
Number of Key Feature Domains Indicated[1]	3 (2,3)	4 (3,4)	1.30 (1.13,1.49)	3 (3,4)	1.25 (1.08,1.47)
≥1 skin feature	88.9	86.7	0.97 (0.85,1.11)	100	1.10 (1.00,1.21)
≥1 respiratory feature	68.9	80	1.16 (0.90,1.50)	94	1.34 (1.06,1.69)
≥1 cardiovascular feature	75.6	84.4	1.12 (0.98,1.28)	71	0.91 (0.47,1.76)
≥1 gastrointestinal feature	13.3	62.2	4.67 (2.21,9.87)	47	3.45 (1.74,6.84)
≥1 neurological feature	8.9	20	2.25 (0.83,6.06)	0	—
≥1 other feature	2.2	2.2	1.00 (0.06,15.98)	17.7	7.8 (0.87,69.58)
Treatment					
Identified appropriate primary treatment	91.1	97.8	1.07 (0.99,1.16)	4	
Indicated appropriate dosage	25	95.3	3.82 (1.90,7.67)	57.9	2.31 (1.23,4.34)
Indicated appropriate route of administration	92.7	100	1.08 (0.99,1.18)	85.7	0.92 (0.78,1.10)
Indicated appropriate route and dosage	19.2	95.3	4.96 (2.26,10.88)	47.6	2.48 (1.21,5.06)
Correctly indicated no contraindications for Epinephrine	85.4	100	1.17 (1.03,1.33)	4	
Practice Cases					
Correctly identified/diagnosed blood transfusion case	97.4	100	1.03 (0.97,1.08)	4	
Correctly identified/diagnosed anaphylaxis case	69.2	90.9	1.30 (1.09,1.56)	4	
Appropriately treated anaphylaxis case	68.9	91.1	1.32 (1.11,1.58)	4	

[1]Median (Interquartile Range) presented along with incidence rate ratios (95% confidence intervals)
[2]Pre vs. post difference estimated with generalized estimating equations specifying Poisson distribution, log link, and robust standard errors
[3]Pre vs. 6-month difference estimated with generalized estimating equations specifying Poisson distribution, log link, and robust standard errors
[4]Comparable question not asked on 6-month follow-up survey

CI 0.98, 1.28). Reporting of gastrointestinal and neurological features was persistently low. All longitudinal respondents were able to identify two or more organ systems as being involved in anaphylaxis, with one-third of residents reporting features across three organ systems, and one-third reporting features across four organ systems.

Knowledge about Diagnosing Anaphylaxis

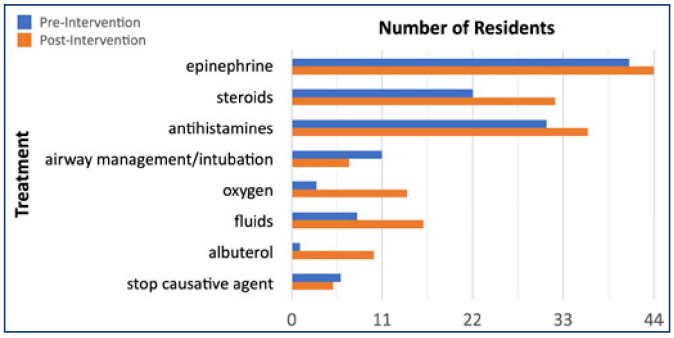
There was an increase from 69.2% to 90.9% of residents who correctly identified the anaphylaxis case among the three patient scenarios after the teaching session (RR: 1.30; 95% CI 1.09,1.56) (**Table 2**). The most common diagnosis among residents who did not categorize the case scenario as anaphylaxis reported that it was an "allergic reaction."

Knowledge about the Treatment of Anaphylaxis

Residents were queried regarding the appropriate pharmaceutical treatment (epinephrine), dosing and route of administration. Prior to the intervention, 91.1% of residents correctly reported treatment with epinephrine; however, only 19.2% of residents were able to correctly state the dose and intramuscular mode of administration of epinephrine prior to the teaching session. This increased significantly to 95.4% immediately post-intervention (RR:4.96; 95% CI: 2.26, 10.88). While the proportion of residents who correctly stated the dose and intramuscular mode of administration dropped to 47.6% on the longitudinal survey, this still represented a twofold improvement compared to pre-intervention (RR: 2.48; 95% CI:1.21,5.06). On a multiple-choice question, 15% of residents initially surveyed incorrectly reported that there are contraindications to giving epinephrine in anaphylaxis. All residents correctly identified that there are no contraindications to the administration of epinephrine for anaphylaxis after the intervention (RR:1.17; 95% CI: 1.03,1.33).

Residents were also asked to list all possible interventions for management of anaphylaxis in an open-ended format (**Figure 2**). Resident responses ranged from critical care interventions such as "intubation" and "vasopressors," to "epinephrine" and "stop causative agent." After the intervention, there was an increased tendency to report prescribing antihistamines and steroids as part of the management of anaphylaxis.

Figure 2. Bar graph demonstrating the number of residents listing each treatment for anaphylaxis on free response, both pre- and post- the instructional session.



DISCUSSION

In this pre- and post-intervention study among residents in a university-based internal medicine training program, we identified specific gaps in knowledge regarding identification and management of anaphylaxis. We demonstrated that a 30-minute teaching session featuring didactic and interactive case-centered learning improved knowledge about the definition of anaphylaxis as an acute, multi-organ system reaction to an allergen, with long-term retention about this potentially fatal syndrome.

Our results indicate successful implementation of a training program in anaphylaxis which can have real-world implications in treatment of anaphylaxis. We directed our teaching efforts towards reinforcing the NIAID definition for anaphylaxis as prior studies have shown that clinicians who do not use this definition are likely to delay treatment.[15] Education surrounding anaphylaxis improved identification of respiratory and cardiovascular symptoms as part of anaphylaxis, which is critical given 10-20% of patients do not present with urticaria, the most prominent, visible feature often identified by providers[23] and due to the significant morbidity and mortality associated with cardiopulmonary symptoms of anaphylaxis which require immediate intervention/escalation of care.

The education emphasized broadening differentials during case conferences to include anaphylaxis, and discussing anaphylaxis treatment in the context of case scenarios to foster timely diagnosis and appropriate management of anaphylaxis.[14] As an example, many hospitals do not provide pre-mixed epinephrine pens on code carts, which can cause mistakes and delays in epinephrine administration, particularly if members of the code team are not familiar with anaphylaxis dosing. Most code carts contain a lower concentration of epinephrine (1:10,000; 0.1 mg/mL) intended for intravenous administration during advanced cardiac life support (ACLS), vs the 1:1000 (1 mg/ml) concentration delivered intramuscularly for anaphylaxis treatment.[24] Responding to anaphylaxis in hospitalized patients requires knowledge of the exact dosing of epinephrine by all members of the healthcare team who may respond to such an emergency. This is important because dosing errors have been shown to lead to serious adverse outcomes.[17]

There is limited research on effective training techniques for teaching anaphylaxis. The European Academic of Allergy and Clinical Immunology (EAACI) Task Force suggests using simulation training to help teach healthcare professionals how to recognize and manage anaphylaxis, although this was based on a small number of randomized controlled trials.[25] Simulation includes the ability to practice administering an epinephrine auto-injector, checking frequent vital signs, and performing an intubation in real time. While simulation cases can be helpful, many hospital settings may not have the resources or funding available to maintain simulation centers and allocate time to all trainees. Our intervention used a slide-based visual presentation and interactive discussion between the peer instructor and residents, making it much more accessible to educators across all clinical settings. Another previously reported teaching intervention on anaphylaxis was conducted via an e-learning module and lecture with multiple-choice survey follow-up, which demonstrated improvement in trainee diagnosis and treatment of anaphylaxis among internal medicine residents.[15] Our study expands on this by incorporating case-based discussions and assessing qualitative responses of participants, which may be more likely to engage learners and reinforce relevant critical decision-making over purely lecture-based instruction.[26]

A strength of this study was the collection of both qualitative and quantitative data, allowing for a more holistic understanding of residents' knowledge base. Additionally, as noted, the teaching session was brief and did not require the use of complex simulation centers or technology, making it feasible, portable and adaptable for use in various educational settings. Limitations include a single-center design among trainees of one specialty and low long-term follow-up response rate. We did not have a control arm to reflect secular changes in knowledge during the study period. Given the post-intervention assessment was administered immediately following the teaching session, observed changes in knowledge were attributed to the intervention, though this assumption does not hold for the longitudinal follow-up. Future studies may focus on modifying the teaching intervention to better highlight the systemic definition of anaphylaxis and earlier implementation of the intervention for residents in their first year of training, so that they may incorporate and practice the clinical skills learned over the course of their residency.

CONCLUSION

Our study demonstrates that a focused didactic and case-based discussion session is effective in immediately improving residents' understanding of the diagnosis and management of anaphylaxis, an acute-onset, potentially fatal condition, and can have long term efficacy.

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Disclosures

Acknowledgments: Resources for this project were provided by the Brown Clinical Educator Track, the Department of Internal Medicine and the Division of Pulmonary, Critical Care, and Sleep Medicine. We thank Dr. Anupama Menon at the Providence Veterans Affairs Medical Center and the 2020-2021 Brown Internal Medicine Chief Medical Residents for their helpful input on the teaching intervention and on this project. An initial analysis of this data was presented as a poster at the Warren Alpert Medical School Medical Education Scholarship Session in Providence, Rhode Island in May 2021.

Supplemental material: Lecture slides, case presentation materials, appendices, and assessment tools are available upon request.

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