

Impact of quality improvement measures on the delivery of allergy immunotherapy: a 2-year follow-up

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Background: Anaphylaxis is the most serious potential complication from allergy treatment with subcutaneous immunotherapy (SCIT). Quality measures were developed with the goal to decrease the incidence of complications resulting from SCIT and improve the safety of care provided.

Methods: The incidence and characteristics of anaphylaxis episodes resulting from SCIT was measured between 2008 and 2012 prior to implementation of quality measures including vial verification, vial testing, and standardized training across 6 allergy delivery sites. Errors and anaphylaxis rates were then tracked prospectively over a 2-year period after implementation of these process measures.

Results: From 2008 to 2012 there were 9 episodes of anaphylaxis or 0.02% of injections/year. Eight patients had sufficient information from which to derive meaningful data. Patient identification error led to anaphylaxis in 2 patients, dosing error in 2, and compounding error in 1 patient. In 2 patients, anaphylaxis occurred with advancement during pollen season, and in 1 patient no clear reason could be

identified although she had asthma as a risk factor. After implementation of quality improvement measures the anaphylaxis rate fell to 0 of 8948 injections for years 2013 and 2014.

Conclusion: Errors in the mixing and administration of allergy serum comprised the majority of identifiable factors that led to anaphylaxis. Implementation of quality measures, including vial verification and vial testing, can improve safety and decrease anaphylaxis rates in the delivery of allergy immunotherapy. © 2015 ARS-AAOA, LLC.

Key Words:

patient safety; anaphylaxis; immunotherapy; allergy; quality metrics

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Allergic disease is a common condition in the United States. Over 50 million Americans are affected by asthma and allergic rhinitis (AR).¹⁻⁴ A recent study of the National Health and Nutrition Examination Survey (NHANES) found that the prevalence of atopy has nearly doubled over the past 20 to 30 years.¹ These diseases im-

pose significant costs on society, with AR alone contributing \$11.2 billion in healthcare expenditures in 2005, leading to 3.5 million lost workdays, and 2 million lost school days.^{1,5,6} An important treatment modality of AR is subcutaneous immunotherapy (SCIT). SCIT decreases allergic symptoms, medication use, improves quality of life measures, and also has the potential to prevent new sensitizations and the development of asthma.⁷ While SCIT is an accepted and generally safe treatment modality for AR, there are possible serious associated complications including anaphylaxis and death.⁸ Prior to 2002, there were an estimated 3.4 fatal reactions per year related to SCIT, and although these numbers appear to be declining, serious systemic reactions still occur in 0.1% of all SCIT administration.⁹ With an increasing need for improved quality and safety in the delivery of allergy care, quality measures were developed with the goal of decreasing or eliminating this potentially life-threatening complication from SCIT. By analyzing rates of anaphylactic reactions before and after implementation

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of quality safety measures, we were able to determine if quality improvement measures changed complication rates from SCIT.

Patients and methods

The incidence and characteristics of anaphylaxis episodes resulting from SCIT were studied between 2008 and 2012, prior to implementation of quality measures. These years were chosen due to lack of available data for prior years. In November 2012, substantial changes to the allergy program were made including standardization of training and delivery of care. Some examples include the implementation of 2-person vial verification, vial testing of all patients across 6 allergy delivery sites, and the centralization of serum compounding. Errors and anaphylaxis rates were then tracked prospectively over a 2-year period after implementation of these process measures. Anaphylaxis was defined as a systemic reaction resulting from immunotherapy administration involving the skin, respiratory tract, gastrointestinal, cardiovascular, and/or neurologic systems.

Vial verification was performed by 2 trained allergy technicians prior to administration of serum to ensure that the correct patient received the correct allergen vial during SCIT administration. This was performed in addition to vial verification by the patient. Vial testing was performed by injecting 0.01 mL of allergy serum intradermally and evaluating the patient response prior to providing the full dose. This important safety check was implemented for the first dose of each vial to identify potential mixing errors and potency changes between antigen lots. If the vial test reaction was less than 13 mm, patients were given the injection with the full dose. If greater than 13 mm, the patient's serum was either held or diluted based on physician recommendation.

Standardized allergy training consisted of Internet-based training modules regarding immunotherapy fundamentals, allergy testing, serum preparation, immunotherapy injections, and anaphylaxis. Yearly training was made a requirement as well as written certification by the physician overseeing the allergy practice on the competency of the allergy technician for both knowledge and safe practices in compounding and administration of allergy immunotherapy. Mock anaphylaxis drills were performed on a quarterly basis, and biweekly educational teleconferences were conducted across all satellites. Due to concerns for significant interruptions during compounding of serum, technicians and nurses were ensured protected time during compounding of serum. Furthermore, checklists were developed for audits of allergy satellites, including availability of proper equipment and medications to manage anaphylaxis, appropriate maintenance and provision of allergy serum, and adherence to protocol for safe delivery of allergy care.

TABLE 1. Grading criteria used in the AAAAI/ACAAI immunotherapy safety survey*

Grade	Reaction	Description of criteria
Grade 1	Mild SR	Generalized urticaria and/or upper respiratory symptoms (eg, itching of the palate and throat, sneezing)
Grade 2	Moderate SR	Asthma (eg, PEFR falls 20% to 40%) with or without generalized urticaria, upper respiratory symptoms, or abdominal symptoms (nausea, cramping)
Grade 3	Severe life-threatening anaphylaxis	Severe airway compromise because of severe bronchospasm (eg, PEFR falls more than 40%), or upper airway obstruction with stridor and/or hypotension

*From Cox et al.¹⁰

AAAAI = American Academy of Allergy, Asthma & Immunology; ACAAI = American College of Allergy, Asthma & Immunology; PEFR = peak expiratory flow rate; SR = systemic reaction.

Results

During the period 2008 to 2012 there were 9 episodes of anaphylaxis, or 0.02% of injections per year. Eight patients had sufficient information from which to derive meaningful data. For the 1 remaining patient, our review shows that an anaphylactic reaction occurred, but we have no available data as to discern an etiology for the reaction. Table 1 shows the characteristics of anaphylactic reactions as graded by the World Allergy Organization.¹⁰ All of our patients experienced at least a Grade II reaction based on the available data. Some patients may have met criteria for a Grade III reaction, but we have no available objective data on physical findings such as uvular or laryngeal edema, etc. There were no Grade IV or V reactions. One of the patients was on a selective beta-blocker at the time of their reaction; none were taking an angiotensin-converting enzyme (ACE) inhibitor. Patient identification error led to anaphylaxis in 2 patients. In both of these cases, the patient received an injection from the wrong vial and the patient name was not checked prior to immunotherapy administration. Dosing error led to anaphylaxis in 2 cases. In the first case, 0.5 mL of the dilution was given instead of 0.15 mL. In the second case, the patient had an injection from a new vial and was advanced incorrectly to the full dose. One patient suffered a systemic reaction due to a compounding error in which the serum was incorrectly mixed at a more concentrated dilution than prescribed. In 2 patients, anaphylaxis occurred with advancement during peak pollen season. One of these patients was undergoing home immunotherapy. Finally, in 1 patient no clear reason could be identified, although she had asthma as a risk factor. The patient had mild intermittent asthma which was well controlled. We routinely screen patients with asthma using spirometry and peak flow measures. None of the patients

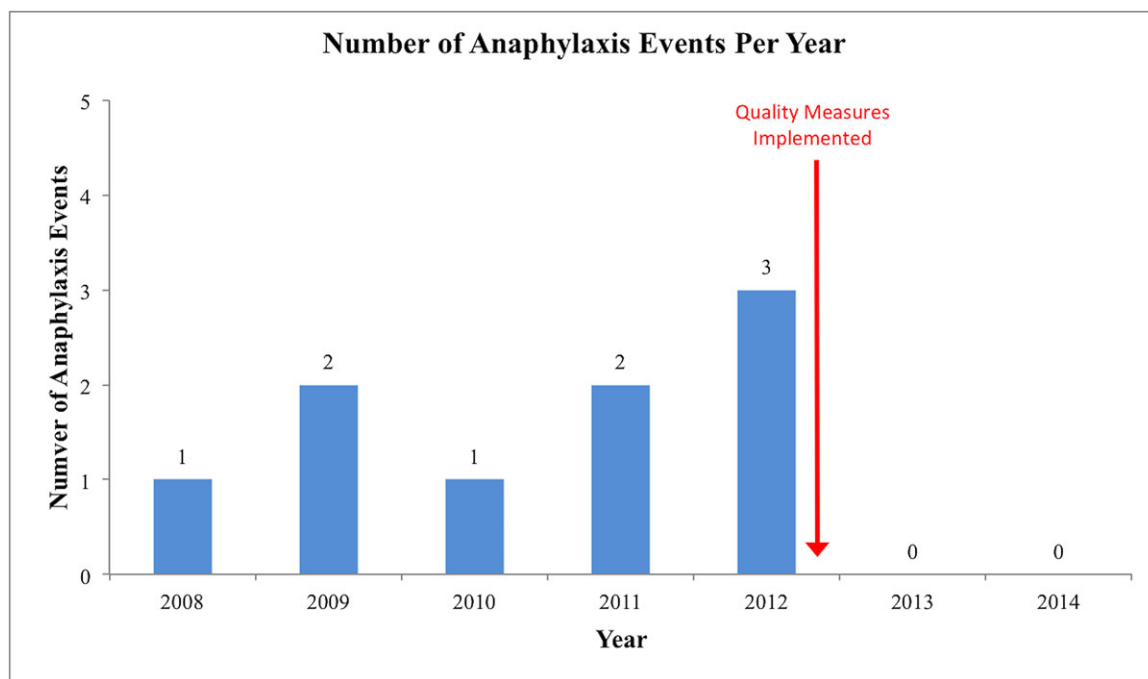


FIGURE 1. Number of anaphylaxis events per year. Illustrates the substantial reduction in yearly anaphylactic events after implementation of quality measures.

with a new vial resulting in anaphylaxis underwent vial testing prior to administration. Six (75%) patients were in the process of being advanced in their immunotherapy. Five (63%) patients had local reactions preceding their systemic reaction. The average time to anaphylaxis was 21 minutes; however, there was a wide range, encompassing 5 to 75 minutes, with most episodes occurring between 10 and 20 minutes after administration. There were no biphasic reactions. All patients had an epinephrine autoinjector (EpiPen). After implementation of quality improvement process measures the anaphylaxis rate fell to 0 of 8948 injections administered during the year 2013, and 0 of 6874 injections administered during the year 2014 (Fig. 1). We continue to track any systemic reactions related to immunotherapy administration.

Discussion

SCIT administration remains an important part of the treatment of AR, and while generally considered a safe modality of treatment, important complications can develop. Of these, anaphylaxis is the most serious.⁵ Although rare, these events continue to occur nationwide.^{1,5,9} Despite the potential for serious complications, there is a paucity of quality evidence on safety and quality of immunotherapy administration. The most recent allergen immunotherapy practice parameters published by the American Academy of Allergy, Asthma & Immunology (AAAAI) and American College of Allergy, Asthma & Immunology (ACAAI) in 2011 reveal that the majority of recommendations regarding safety are C or D in strength, meaning that the available data is mostly descriptive or based on expert opinion.¹¹

In the most recent AAAAI/ACAAI surveillance study, a fatal reaction from SCIT was reported, which had occurred in 2009. The cause of death was due to severe upper airway angioedema and hypotension despite fluid resuscitation and emergent tracheostomy.⁹ This report revealed several potential contributors to this patient's event, which included: (1) significant hypersensitivity to weeds but continued advancement during peak weed season; (2) recent ACE inhibitor therapy; and (3) administration of epinephrine subcutaneously instead of the preferred intramuscular route. He had no prior history of systemic reactions, and while he had a history of asthma, it was considered to be adequately controlled.⁹ It should be noted that while advancement during peak season, ACE inhibitor use, and asthma control are potential contributors to the patient's reaction, these are based on Level III or IV evidence in the literature.¹¹ In this fatal case a dose error was ruled out, but it is unclear whether vial testing was performed from the report. Although it is impossible to know whether this episode could have been prevented, it does illustrate that the event occurred in the setting of some preventable oversights in SCIT administration. Situations like the one described above show the need for stringent quality measures in immunotherapy delivery. Additionally, new legislation such as the Drug Quality and Security Act demands that practitioners who compound medications in the office also follow U.S. Pharmacopoeia regulations.¹² This increases the responsibility of the provider to adhere to strict measures of safety and quality in the compounding of immunotherapy, in addition to its administration.

Review of our data between the years of 2008 and 2012 revealed that the majority of systemic complications were

secondary to avoidable causes. Namely, these were errors in patient identification, allergen dosing, vial compounding, and dose advancement during peak allergen season, all of which were potentially preventable. The implementation of patient vial verification, vial testing, and standardized allergy training across all of our immunotherapy sites eliminated the occurrence of systemic reactions. Because of our center's experience in which 2 patients experienced an anaphylactic reaction during peak season, we additionally implemented dose reductions during this time. While our follow up is limited to 2 years, this study demonstrates that a systemwide implementation of immunotherapy delivery standards can significantly reduce the occurrence of danger-

ous and life-threatening reactions to SCIT. More prospective studies are needed to determine efficacious interventions that promote patient safety, quality, and outcome.

Conclusion

Errors in the mixing and administration of allergy serum comprised the majority of identifiable factors that led to anaphylaxis in our population. Implementation of quality measures in our prospective analysis of anaphylaxis rates, including vial verification and vial testing, improved safety and decreased anaphylaxis rates in the delivery of SCIT. 

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