

Single-Step Venom Allergy Testing

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Practice Options from Beyond Our Pages focuses on identifying, critiquing, and placing into context research studies published in other journals that have the potential to change our clinical practices. It is written by Allergy-Immunology Fellows partnered with faculty members, and does not require an invitation for submission. This feature is coordinated by Editorial Board members Matthew Rank, MD and Julie Wang, MD.

REFERENCE

Quirt J, Wen X, Kim J, Herrero A, Kim H. Venom allergy testing: Is a graded approach necessary? *Ann Allergy Asthma Immunol* 2016;116:49-51.

BACKGROUND

It is estimated that systemic, life-threatening reactions to insect stings occur in up to 3% of the adult population and 0.4% to 0.8% in the pediatric population.^{1,2} Currently, it is recommended that patients with a history of systemic reaction to venom be evaluated for venom sensitization because 30% to 60% of patients will have a subsequent systemic reaction if re-stung.² These patients are candidates for venom immunotherapy (VIT), because VIT has been shown to reduce the risk of future systemic reactions to less than 5%, with future sting reactions typically being milder.² On the basis of a 2016 American Academy of Allergy, Asthma & Immunology (AAAAI) practice parameter update on stinging insect hypersensitivity, adults and children with cutaneous only manifestations of a systemic reaction are at a low risk for future systemic reactions and, outside of special circumstances, are not candidates for VIT.²

In patients who are candidates for VIT, current American Academy of Allergy, Asthma & Immunology practice parameters recommend performing skin tests and/or specific IgE to evaluate for venom sensitization. A commonly used protocol for intradermal testing begins with venom concentrations of 0.001 to 0.01 µg/mL, increasing by 10-fold every 20 minutes until a maximum concentration of 1 µg/mL is reached or a positive test result. All commercially available extracts for vespid and bee venoms should be used.²

Regardless of the age of the patient, testing for venom allergy is time consuming and may cause significant discomfort. The article reviewed here proposes a 1-step intradermal protocol that

was safe and effective in the diagnosis of hymenoptera venom allergy.³

METHODS

This was a retrospective chart review evaluating 300 consecutive patients who were evaluated at a single allergist's practice in Canada that had implemented a single-step hymenoptera venom allergy testing protocol. All patients had suspected systemic reactions to at least 1 sting and had at least 1 positive reaction on intradermal testing. Patient information collected included age, sex, reaction severity, medications, testing protocol used, and venom positivity on testing. Adverse reactions occurring at the time of testing or any delayed reactions were reported to the allergist and recorded.

The testing protocol that was used for all patients consisted of a single intradermal injection of 0.02 mL at a concentration of 1.0 µg/mL of each of 5 Hollister-Stearns available bee and vespid venom extracts, which included yellow jacket, yellow hornet, white-faced hornet, honeybee, and paper wasp. Epicutaneous skin testing was not performed. A positive reaction was a wheal of at least 7 mm with a flare.

RESULTS

Mean patient age was 42 years, with a range of 4 to 83 years. A total of 164 (55%) patients were male. Patients taking angiotensin-converting enzyme inhibitors (8.3%), angiotensin receptor blockers (4.7%), and beta-blockers (3.7%) were included in the study. Patients had varying degrees of initial reaction severity, with 40.7%, 15%, 20%, and 24.3% of patients having a history of grade 1, 2, 3, and 4 reactions, respectively, with grade 1 being the mildest and grade 4 being the most severe.⁴ Most patients had positive testing to more than 1 venom, and nearly all patients were positive to yellow jacket (n = 265 of 300 [88%]). A total of 193 of 300 patients (64%) showed positivity to yellow hornet, 115 to wasp (38%), 198 to white-faced hornet (66%), and 16 to honeybee (5%). Of those with single-venom positivity, yellow jacket was the most common (n = 71 of 300 [23.7%]), followed by honeybee (n = 8 of 300 [2.7%]), white-faced hornet (n = 6 of 300 [2%]), wasp (n = 3 of 300 [1%]), and yellow hornet (n = 1 of 300 [0.3%]).

There were no immediate adverse reactions to single-step venom testing. One patient had a delayed adverse reaction. He was a 34-year-old man with an initial reaction to an unknown insect that included immediate lip swelling, shortness of breath, and tachycardia. His skin testing was positive to yellow jacket, yellow hornet, and white-faced hornet. He was not taking a beta-blocker, an angiotensin-converting enzyme inhibitor, or an angiotensin receptor blocker. He was asymptomatic immediately

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after testing; however, upon waking the morning after testing, he had generalized urticaria with pruritus with no other symptoms. He subsequently tolerated venom immunotherapy. No other adverse events were reported.

CRITICAL APPRAISAL

Data from this study show that single-step venom testing with a single, maximum dose administered via the intradermal route can be considered a safe and effective diagnostic tool in hymenoptera allergic patients. The use of this approach limits the time required for testing, cost of testing, and discomfort for patients. Only 1 adverse reaction was documented in this study, which was delayed, and thus would have likely occurred regardless of the method used for testing. Therefore, the risk of a systemic reaction with the 1-step venom allergy testing approach is less than 1:300. This is reassuring because the risk of a systemic reaction to allergen immunotherapy is estimated to be approximately 0.2% per injection with conventional schedules.⁵

The rationale for a stepwise approach is due to the perceived risk of a systemic reaction with skin testing.³ However, systemic reactions to venom skin tests are rare and are not more frequent with accelerated testing methods.² This study supports this by demonstrating the safety of accelerated testing on patients with varying degrees of initial reaction severity, including 24.3% of patients with an initial grade 4 reaction.³ Other studies have similarly shown the safety of accelerated methods for venom skin testing.^{6,7} The American Academy of Allergy, Asthma & Immunology stinging insect hypersensitivity practice parameters 2016 update remarks on these studies but does not specifically recommend utilization of the accelerated versus the standard approach previously described for venom skin testing.²

Although this study did include patients on angiotensin-converting enzyme inhibitors and beta-blocker therapy, the total number of patients on these medications was small, so further studies may be needed to determine whether an accelerated method is safe in this population. This study also included a low percentage of patients who were honeybee allergic, and therefore safety in populations with higher percentages of honeybee-allergic individuals may be less certain. In addition, although this study did include pediatric patients, this was not a

specific pediatric study and the exact number of pediatric patients is not reported. Given the mean age of 42 years, it was likely an adult-predominant cohort and results may not be generalizable to pediatrics. However, a recent study by Cichocka-Jaros et al⁸ demonstrated clinical safety with higher concentration intradermal venom skin testing in children ($n = 91$) with no reported systemic reactions, suggesting that eliminating low venom concentration intradermal testing may be safe in children as well. However, they did not include all venoms available for testing in the United States so results may not be generalizable.⁸

RECOMMENDATION

A modified, single-step protocol for evaluating hymenoptera venom allergy via intradermal skin tests may be considered in hymenoptera venom allergic patients because it has been shown to be safe and effective in the diagnosis of hymenoptera venom allergy. Its use in patients on angiotensin-converting enzyme inhibitors or beta-blocker therapy, those who are honeybee allergic, as well as pediatric patients is not as well studied but evidence indicates that it may also be safe in those populations.

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