

Contents lists available at [SciVerse ScienceDirect](#)

Adherence to imported fire ant subcutaneous immunotherapy

Shayne C. Stokes, MD; James M. Quinn, MD; Joshua J. Sacha, DO; and Kevin M. White, MD

Division of Allergy and Immunology, Department of Medicine, Wilford Hall Medical Center, San Antonio, Texas

ARTICLE INFO

Article history:

Received for publication July 31, 2012.

Received in revised form October 31, 2012.

Accepted for publication November 17, 2012.

ABSTRACT

Background: Imported fire ant (IFA) subcutaneous immunotherapy (SCIT) is safe and effective. For optimal protection, SCIT is given monthly for 3 to 5 years. Successful outcomes require patient adherence.**Objective:** To evaluate SCIT adherence in IFA allergic patients in an endemic area.**Methods:** Patients with systemic reactions to an IFA sting, with detectable specific IgE, who received a recommendation to start IFA SCIT were included. Initial reaction severity and demographic data were collected. Patients were contacted at 1 year regarding interval reactions to stings, SCIT adherence, and reason for nonadherence. Adherence rates were analyzed for association with age, sex, and severity of initial reaction.**Results:** Seventy-six patients were enrolled, and 71% adhered to the recommendation to start IFA SCIT. Subgroup analysis did not find significant differences. At 1 year, 97% completed follow-up for analysis, and only 35% remained adherent. Subgroup analysis did not find significant differences. Inconvenience and fear were reported as reasons for not following the recommendation to start or continue with IFA SCIT.**Conclusion:** IFA SCIT is a life-saving therapy that is safe and effective. Despite this, only 71% followed the recommendation to start, and at 1 year only 35% remained adherent. Adherence was not statistically related to age, sex, or severity of initial reaction. Logistical constraints and fear were significant impediments.

© 2013 American College of Allergy, Asthma & Immunology. Published by Elsevier Inc. All rights reserved.

Introduction

The imported fire ant (IFA), first introduced into the United States through the port of Mobile, Alabama, in the early 1900s,¹ continues to be responsible for considerable morbidity and rare fatalities. IFAs are now common throughout the southeastern United States and are expected to continue to spread. Sting attack rates have been reported to be as high as 50% for even brief stays in endemic areas.² In addition, a survey of physicians reported treatment of more than 20,000 patients annually for symptoms related to IFA stings,³ with up to 16% requiring treatment for systemic reactions.⁴ Although rare, at least 84 fatal reactions have been reported to IFA stings.⁵

IFA subcutaneous immunotherapy (SCIT) is an effective, potentially life-saving treatment. It is currently the only disease-modifying treatment available and has been reported to significantly decrease the risk of systemic reactions to subsequent stings.⁶ For optimal protection, IFA SCIT should be continued for at least 3 to 5 years.⁷

Successful clinical outcomes require both a commitment to initiate and sustained adherence to the prescribed SCIT regimen.

Reprints: Shayne C. Stokes, MD, Allergy and Immunology Division, Department of Medicine, Wilford Hall Medical Center, 2200 Bergquist Dr, Suite 1, Lackland Air Force Base, San Antonio, TX 78236; E-mail: shayne.stokes@us.af.mil.

Disclosures: Authors have nothing to disclose.

Disclaimer: The opinions or assertions herein are the private views of the authors and are not to be construed as reflecting the views of the US Department of the Air Force or the US Department of Defense.

Funding Sources: This study was supported by the US Air Force.

Nonadherence to medical therapies is a frequently encountered problem, especially when dealing with prophylactic or suppressive treatments.⁸ In fact, studies examining aeroallergen SCIT have reported nonadherence rates as high as 50%.⁹ Only one study has specifically reported on adherence to IFA SCIT.¹⁰ This retrospective review defined adherence as having received any injection within the preceding 3 months and reported an adherence rate of 64%. There are no published prospective data regarding adherence with the recommendation to initiate and then to continue with IFA SCIT.

The purpose of this study was to assess how patients, in a highly endemic area, adhered to the recommendation to initiate IFA SCIT and then, in a prospective manner, to follow up patient adherence once SCIT was initiated. In addition, we analyzed specific factors that might affect patient adherence to this potentially life-saving therapy.

Methods

The study protocol was approved by the Wilford Hall Medical Center (WHMC) institutional review board. Written informed consent was obtained for each enrollee before beginning IFA SCIT. Enrollees were informed that they would be contacted 1 year after enrollment to inquire about their IFA SCIT course, interval IFA stings, and reactions to interval stings. They were not informed that their specific adherence would be assessed. The benefits of IFA SCIT, including a significant reduction in the risk of systemic reactions to subsequent IFA stings and a sustained risk reduction after completion of a 3- to 5-year SCIT course, were explained in detail to

Table 1
Baseline characteristics of the study participants

Characteristic	No. (%) of patients (N = 76)
Child (<17 years old)	14 (18)
Adult (≥17 years old)	62 (82)
Male	31 (41)
Female	45 (59)
Grade I initial reaction	13 (17)
Grade II initial reaction	58 (76)
Grade III initial reaction	5 (7)

each patient by their primary allergist at the time of their enrollment. As part of this discussion, each allergist reviewed the requirement for adherence to both build-up and maintenance phases of IFA SCIT to achieve the protective benefit. All patients were offered the option of a rush vs conventional build-up and were allowed to select the build-up method of their choice.

Patients who were referred to the WHMC for evaluation of reactions to IFA stings were considered for enrollment. All enrolled patients had a history of an IFA sting that resulted in a systemic reaction and IFA specific IgE detected by ImmunoCAP (>0.35 kU/L) and/or skin testing (positive response at ≤1:1,000 wt/vol by the skin prick or intradermal method). In addition, each patient received an allergist's recommendation to begin IFA SCIT and had IFA whole-body extracts ordered.

Demographic data, including the severity of the patient's initial reaction, age, and sex, were collected from a medical record review. The reaction severity was classified as grade 1 if the reaction was isolated to skin and subcutaneous tissues; grade 2 if respiratory, cardiovascular, and/or gastrointestinal symptoms were present; and grade 3 for hypoxia, hypotension, or neurologic compromise.¹¹ Patients were categorized into the child subgroup if they were younger than 17 years and the subgroup adult if they were 17 years or older. Patients younger than 17 years with isolate grade 1 reactions were excluded.

We defined adherence to IFA SCIT initiation as having received at least one injection. Adherence to continuation was defined as still receiving IFA SCIT at 1-year follow-up. All patients who remained adherent at 1 year had completed build-up and were receiving their maintenance dose. Patients were contacted by telephone or e-mail 1 year after enrollment, and a questionnaire was used to assess adherence to IFA SCIT initiation and continuation and to document reasons for nonadherence. Nonadherent patients were counseled on the risk of systemic reactions without IFA SCIT and the protective benefit offered by adherence to their

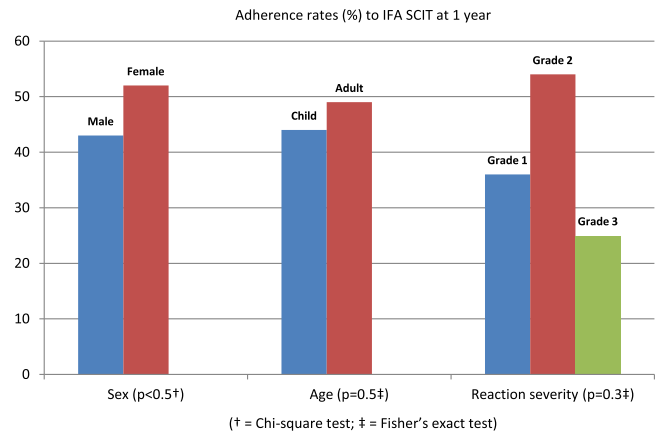


Figure 2. One year adherence rates by subgroup.

prescribed IFA SCIT regimen. Nonadherent patients were offered a follow-up appointment to discuss restarting IFA SCIT. Immunotherapy records were reviewed to validate patient responses. Adherence was then analyzed for association with build-up regimen, age, sex, and initial reaction severity using a Fisher exact test or χ^2 test.

Results

The baseline characteristics of our 76 enrolled patients are listed in Table 1. Adult patients made up 82% of our cohort, with 59% being female. Most of our patients (76%) had grade 2 initial reactions, with 17% reporting grade 1 and 7% reporting grade 3 initial reactions.

Of our 76 patients, 54 (71%) were adherent to the recommendation to initiate IFA SCIT (Fig 1). Subgroup analysis revealed no statistically significant differences between male and female patients, children and adults, the severity of the initial reaction, and the likelihood of initiating immunotherapy.

A rush build-up regimen was chosen by 47 of our 76 patients (62%). Despite the convenience of using a 1-day rush build-up protocol, only 37 (79%) were adherent with initiation. The remainder of the patients chose a conventional build-up regimen, with 17 of 29 (59%) being adherent with initiation. Statistical analysis revealed no significant differences regarding adherence with initiation when comparing those who chose a rush vs a conventional build-up regimen.

At 1-year follow-up, only 26 of the 54 patients (48%) who started immunotherapy were still receiving IFA SCIT (Fig 2). These

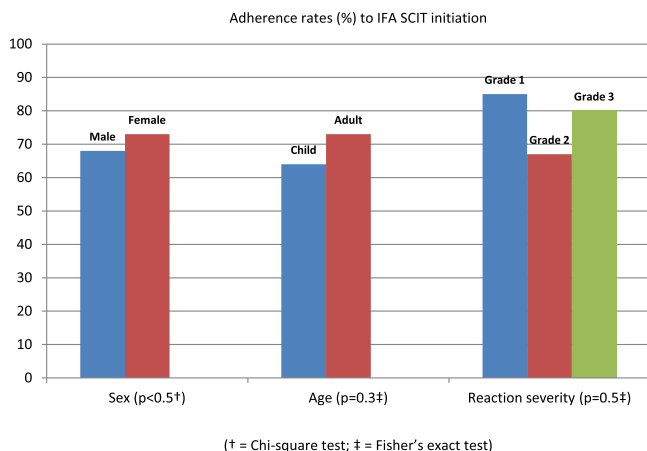


Figure 1. Initiation rates by subgroup.

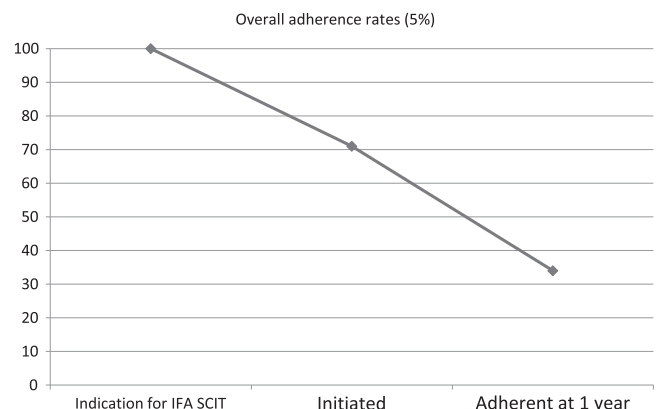


Figure 3. Overall adherence rates.

Table 2

Reasons for patient nonadherence to treatment

Reason for nonadherence	With initiation, %	With continuation, %
Inconvenience	50	54
Needle phobia	28	25
Other	22	21

26 patients had all successfully reached their maintenance dose and were continuing to receive their recommended IFA SCIT maintenance injections. Subgroup analysis found no statistically significant difference between male and female patients, children and adults, the severity of the initial reaction, rush vs conventional build-up, and the likelihood of still receiving immunotherapy at 1 year. Ten patients in our cohort moved to a new military treatment facility before their 1-year follow-up. Six of these patients remained adherent at 1 year. No significant difference was found between the schedule and travel issues in the 10 patients who moved to a new facility and the remainder who continued to receive care at the initial military referral center.

Figure 3 shows the overall adherence rates for all patients who should have been receiving IFA SCIT, including both those who did and did not follow the recommendation to initiate. We obtained 1-year follow-up on 74 of 76 (97%) of our initial patients at which time only 26 of the 74 patients (35%) who should be receiving IFA SCIT remained adherent. Subgroup analysis found no statistically significant differences in each of the subgroups and the likelihood of remaining adherent at 1 year. Patients were also asked to state their most important reason for not starting or not continuing IFA SCIT. Inconvenience and needle phobia accounted for most answers (Table 2).

Discussion

A successful response to immunotherapy requires a commitment by the patient to initiate the prescribed regimen and then to continue appropriate interval SCIT injections. Poor adherence to aeroallergen SCIT is not uncommon and may be due to the elective nature of the therapy, inconvenience, or adverse reactions to the injections.^{12,13} Only one study has specifically reported on adherence to Hymenoptera SCIT.¹⁰ This retrospective review defined adherence as having received any injection within the preceding 3 months and reported an adherence rate of 83% for flying Hymenoptera SCIT. There are no published prospective data regarding adherence to the allergist's recommendation to initiate and then to continue with the prescribed Hymenoptera SCIT regimen.

We evaluated adherence to a potentially life-saving therapy in patients living in an area at high risk for repeat exposures to IFA stings and found that most fail to follow the recommended treatment plan. Only 71% of patients with an indication for IFA SCIT followed the allergist's recommendation to initiate IFA SCIT, and only 35% remained adherent at 1 year. The severity of the patient's initial reaction, age, sex, or build-up schedule did not predict the likelihood of adherence. Inconvenience and fear seem to be significant impediments.

Our study was performed at a military referral center. All initial evaluations, IFA SCIT extract orders, and IFA SCIT build-up were

initiated at a single center. We have attempted to create a system that minimizes schedule and travel difficulties for our patients. After initiation, patients could choose to receive their ongoing IFA SCIT injections at 1 of 2 geographically separated military allergy clinics on opposite sides of the city of San Antonio, Texas. Both clinics were open for immunotherapy injections Monday through Thursday from 7:30 AM to 3:30 PM, with one clinic also being open Friday from 7:30 to 11:30 AM. Our mean patient wait from check-in to injection is approximately 10 minutes, depending on the number of immunotherapy patients presenting at any given time. In addition, our population is unique in that many of our patients transfer locations according to the needs of the military. A system is in place to make SCIT fully portable as patients transfer among different military treatment facilities. This system is designed to minimize interruptions in therapy in a population that is inherently mobile. We believe that these accommodations have maximized our ability to address patient schedule and travel concerns, to support our mobile population, and to make immunotherapy as convenient as is reasonably possible. Despite these accommodations, most of our patients did not adhere to the recommended treatment plan.

Our findings suggest that even though we have a potentially life-saving therapy with proven safety and efficacy and have attempted to minimize obstacles, adherence to IFA SCIT remains problematic. Although this was a single-center study, we believe that this knowledge can make physicians aware of the potential for poor adherence to IFA SCIT and provide an opportunity to consider logistical challenges and to maximize patient education regarding the risks and benefits of IFA SCIT to improve adherence. Additional studies are needed to compare IFA SCIT adherence rates among centers and to identify best practice procedures to maximize adherence.

References

- [1] Lofgren CS, Banks WA, Glancey BM. Biology and control of imported fire ants. *Annu Rev Entomol*. 1975;20:1–30.
- [2] Tracy JM, Demain JG, Quinn JM, et al. The natural history of exposure to the imported fire ant (*Solenopsis invicta*). *J Allergy Clin Immunol*. 1995;95:824–828.
- [3] Stafford CT, Hutto LS, Rhoades RB, et al. Imported fire ant as a health hazard. *Southern Med J*. 1989;82:1515–1519.
- [4] Tankersley MS. The stinging impact of the imported fire ant. *Curr Opin Allergy Clin Immunol*. 2008;8:354–359.
- [5] Rhoades RB, Stafford CT, James FK Jr. Survey of fatal anaphylactic reactions to imported fire ant stings. *J Allergy Clin Immunol*. 1989;84:159–162.
- [6] Freeman TM, Hylander R, Ortiz A, et al. Imported fire ant immunotherapy: Effectiveness of whole body extracts. *J Allergy Clin Immunol*. 1992;90:210–215.
- [7] Golden DBK, Moffitt J, Nicklas RA, et al. Stinging insect hypersensitivity: a practice parameter update 2011. *J Allergy Clin Immunol*. 2011;127:852–854.
- [8] Blackwell B. Patient compliance. *N Engl J Med*. 1973;289:249–252.
- [9] Cohn JR, Pizzi A. Determinants of patient compliance with allergen immunotherapy. *J Allergy Clin Immunol*. 1993;91:734–737.
- [10] More DR, Hagan LL. Factors affecting compliance with allergen immunotherapy at a military medical center. *Ann Allergy Asthma Immunol*. 2002;88:391–394.
- [11] Brown SGA. Clinical features and severity grading of anaphylaxis. *J Allergy Clin Immunol*. 2004;114:371–376.
- [12] Lower T, Henry J, Mandick L, et al. Compliance with allergen immunotherapy. *Ann Allergy Asthma Immunol*. 1993;70:480–482.
- [13] Tinkelman D, Smith F, Cole WQ, et al. Compliance with an allergen immunotherapy regimen. *Ann Allergy Asthma Immunol*. 1995;74:241–246.