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The safety of self-administered allergen immunotherapy during the buildup and maintenance phases

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Abstract

Background—Self-administered allergen immunotherapy is considered controversial. We believe the implementation of a self-administration protocol characterized by patient preselection and a slow buildup phase is safe.

Methods—We analyzed 23,614 patient records and associated immunotherapy injections for systemic reactions (SR) during a 1-year period (2011 to 2012). SRs were graded in accordance with the World Allergy Organization (WAO) criteria.

Results—Thirty-seven SRs were reported for 23,614 patients who self-administered 2,021,600 injections yielding an annual SR rate of 0.16% (per patient) or 0.002% (per injection). Only 9 of 4643 pediatric (0.19%) and 28 of 18,971 adult patients (0.15%) experienced 1 or more SRs. No deaths (grade V SR) occurred. From 2009 through early 2014, over 90,000 patients received more than 10 million injections in accordance with the United Allergy Services (UAS) protocol without fatalities.

Conclusion—We believe this safety profile is due to a preselection of patients to exclude those with a high risk for adverse reactions and a slow immunotherapy buildup phase. In contrast, previous studies documented office-based SRs ranging from approximately 3% to greater than 14%. Thus, the UAS home-immunotherapy SR rate is significantly lower than office-based immunotherapy SR rates ($p < 0.0001$). The enhanced safety of this protocol results in a decreased frequency and severity of SRs. This safety report, derived from analyses of one of the largest patient cohorts studied, corroborates and expands the observations of previous studies of self-administered subcutaneous immunotherapy in a low-risk patient population by assessing self-administered allergen immunotherapy during the buildup and maintenance phases.

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Keywords

self-administration; allergen immunotherapy; safety; systemic reaction; epinephrine

The only known therapeutic modality that specifically addresses the central pathophysiology of allergic rhinitis (AR) is allergen immunotherapy (IT).[1,2] A course of IT for 3 to 5 years results in significant long-term symptom relief for the majority of patients. Furthermore, IT is known to diminish the severity of allergic asthma and atopic dermatitis and to simultaneously be a steroid-sparing therapy.[3–9] In contrast, the efficacy of pharmacotherapy is strictly limited to the period of active treatment. Unlike pharmacotherapy, IT may also decrease the onset of new allergic sensitizations and development of allergic asthma in both pediatric and adult patients.[3,4]

Although subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) are efficacious, historic safety issues pertaining to SCIT induced systemic reactions (SR) and possible death remain medical concerns. With regard to self-administered SCIT, the criticism of the immunotherapy practice parameters is a reiteration of the 1994 American Academy of Allergy and Immunology (AAAI) position paper.[10] Two key previous surveys are cited as evidence for these recommendations, specifically, Lockey et al.[11] and the UK 1986 Committee on Safety of Medicine (CSM) Update.[12] However, these surveys only document a small percentage of self-administered SCIT-associated fatalities. In fact, the vast majority of reported SCIT-associated fatalities were office-based. Most were “high-risk” patients that would not be considered IT candidates by current standards.[2,13]

Some previous studies have documented the safety of self-administered SCIT that was initiated during the maintenance phase of IT.[14–16] In the current study, based upon the results of possibly the largest cohort study of patients receiving self-administered SCIT, we extend the previous safety results to encompass self-administered IT during both the buildup and maintenance phases of IT.

Patients and methods

United Allergy Services (UAS) facilitates primary care physicians with allergy assessment and therapy. The UAS program is currently used in primary care clinics in 30 states. The protocols and patient screening guidelines and choices of therapy are under the auspices of the primary care physician.

Data collection and reporting

All records pertaining to the treatment of patients are collected and stored in the cloud-based database software, SalesForce (SalesForce.com, Inc., San Francisco, CA). This collection and storage process is Health Insurance Portability and Accountability Act (HIPAA)-compliant; access is both individual and computer restricted and is also password protected. Patients are instructed to report all local reactions and SRs to their physician when they occur. When the report is received, an adverse reaction report, capturing all pertinent information regarding the SR and treatment, is created and upload to the patient’s record and maintained on SalesForce. All SRs and local reactions are further reviewed during clinic

appointments in which dose-logs, analysis of potential adverse events, and the acquisition of the next set of unit-dose vials occurs (see Compliance, below).

This study was reviewed and approved by Salus Independent Review Board (IRB) (Austin, TX). With approval from the Salus IRB, patient records were reviewed for reported SRs. Emergency room (ER) records, if applicable, were requested from the providing physician and uploaded to the patient's record. SRs between 2011 and 2012 were graded in accordance with the World Allergy Organization (WAO) grading criteria (Table 1).[17] Statistical analysis and summaries were performed using SAS version 9.3 (SAS Institute, Inc., Cary, NC). All patient records with reported SRs were identified and analyzed.

The SRs were graded by 3 qualified individuals as per protocol in accordance with the WAO grading criteria (Table 1, grades I through V).[17] Reviewers were blinded to knowledge of patient name and location of medical office and the previous reviewer's designated grade.

Patients

All patients were previously diagnosed with seasonal and/or perennial AR; this encompassed patient history, physical exam, environmental assessment, and the results of allergy skin-prick testing (SPT) as previously recommended.[18] Contraindications to SPT and IT (eg, severe and/or uncontrolled asthma, significant cardiovascular disorders, use of beta adrenergic receptor antagonists, etc.) are consistent with current recommendations.[2] All patients underwent SPT using either the ComforTen (Jubilient Hollister-Stier Laboratories, Spokane, WA) or the Greer Omni (Greer Laboratories, Lenoir, NC) multitest devices with perennial and seasonal geographically relevant extracts consistent with standard practices.[2,19]

Due to the documented increased risk of SRs during the IT buildup phase, the UAS protocol was designed to complete the buildup phase over a 6-month period.[9, 13, 20–22] This results in achieving maintenance concentrations in 6 months rather than the more typical shorter period associated with rush, cluster, and more traditional IT protocols.[2,23] The IT concentrations used are equivalent to the current recommendations (Table 2).[2]

Immunotherapy

Immunotherapy solutions contained allergen extracts defined by patient history, symptomology, environmental exposure, and SPT results. IT formulation also incorporated principles of allergen cross-reactivity, allergen endogenous enzyme activity, and multiallergen extract dilution effects.[24, 25] IT formulation guidelines were in accordance with published recommendations.[2]

The UAS protocol required all patients to undergo initial office-based SCIT, which included education, instruction in the use of epinephrine, and the self-administration of SCIT under the supervision of the physician of record. All office-based SCIT included a 30-minute postinjection observation period. In the event that the patient did not successfully meet required standards for self-administration, IT was continued only on an office-based regimen. All individuals were instructed in the identification and appropriate treatment and response to local reactions and SRs.

For those eligible individuals deemed capable of home IT, by the prescribing physician, further specific requirements were followed. These requirements included: the availability of epinephrine and the presence of an “IT partner” for all injections who was knowledgeable of the IT regimen, vial storage, and the administration of epinephrine, if required. In addition, all IT-induced local reactions and SRs and ameliorating therapy used were to be reported to the clinic as soon as possible. No further SCIT administration was to occur until the clinic was informed and instructions were imparted to the patient, including the need for an office follow-up appointment. In such cases, if IT was to continue, the next several SCIT administrations were to be accomplished at the clinic under the physician’s supervision.

Due to the reported association of SRs occurring after administration of an inappropriate dose,[2] UAS protocols required the patient to receive only 1 set of unit-dose vials monthly from the clinic in order to minimize the risk of such associated SRs. Finally, patients with mild to moderate (but not severe) asthma and under control, as determined by the provider consistent with the 2007 National Heart, Lung, and Blood Institute (NHLBI) Asthma Guidelines, were requested to assess their asthma status prior to SCIT administration.[26]

IT protocol

The UAS self-administration protocol encompasses several subcutaneous injections per week during the buildup phase for 6 months, at which point maintenance dosing is achieved. Subsequently, maintenance doses are administered weekly.

Compliance

To promote safety and compliance, all patients are only given a single unit-dose vial set and a preprinted IT injection log book that enumerates all required doses (eg, volume and frequency of each subcutaneous injection administration) to take home. Patients are instructed to maintain the injection log and to record any pertinent events related to the injections. In addition, patients may additionally use an electronic mobile dosage log, accessed through any device with internet connection. The electronic dosage log uses notifications that let the patient know when they have missed an injection or are due to return to the clinic. When the patients have finished their current unit-dose vial set, they are instructed to return to the clinic with their completed log book for review and to acquire their next unit-dose vial set (every 30 days). During this appointment, injection logs, both paper-based and electronic, are reviewed to check for compliance and any remarks pertaining to injection related events (possible unreported local reactions or SRs).

Results

Patients

A thorough review revealed that 23,614 patients were approved and undergoing self-administered IT during the study period of 2011 to 2012. We identified 37 of these patients who experienced SCIT-associated SRs.

The patients who experienced SCIT-associated SRs consisted of 15 males and 22 females. There were 15 Caucasians, 5 African Americans, 7 Hispanics, and 11 patients who did not

voluntarily identify their ethnicity or race. The pediatric population consisted of 4 Caucasians, 3 Hispanics, 1 African American, and 1 individual who did not voluntarily identify his ethnicity or race. The average age for males was 28 ± 19 years, whereas the average age for females was 40 ± 15 years. For the pediatric population, the average for males was 10 ± 3 years and 10 ± 2 years for females.

Comorbidities included 7 individuals with controlled asthma and 8 patients with controlled hypertension. Three individuals had both asthma and hypertension. Within the pediatric population, 2 males and 1 female had controlled asthma. Duration of IT prior to the SR was 17 ± 12.5 weeks for all patients, and 20 ± 11.7 weeks for males and 15 ± 12.7 weeks for females. This equates to 22 of the 37 (60%) documented SRs occurring during the buildup phase and the remaining 40% occurring during the maintenance phase of IT. Of the patients that experienced an SR, 78% either were instructed to or voluntarily ceased their IT.

IT dosing

Table 2 shows a comparison of the UAS initial annual cumulative dosing during the 6 months of the buildup phase plus the 6 months of maintenance vs the recommended practice parameters cumulative dose achieved during the buildup and maintenance phases (4 months of buildup and 8 months of maintenance).[2] The presented standardized allergen extract doses enumerated in Table 2 are for the most common allergens used in SCIT formulations during the period of study.

Safety

Thirty-seven SRs were reported for 23,614 patients undergoing home-based SCIT, which yielded an SR of 0.16% (per patient). These patients were administered 2,021,600 injections, using the UAS protocol, which was associated with an SR rate of 0.002% (per injection). Adult patients who underwent IT numbered 18,971 and were administered 1,624,135 injections. The resultant SR rates were 0.15% per patient and 0.002% per injection.

Pediatric patients numbered 4643 individuals (5 to 17 years of age) and were administered 397,466 injections. The pediatric SR rates were 0.19% per patient and 0.002% per injection.

The documented 37 SRs were 18 grade I (13 female), 17 grade II (7 female), 1 grade III (female), and 1 grade IV (female). No grade V reactions occurred in over 2 million self-administered injections (see Fig. 1). Pediatric SRs consisted of 3 grade I and 4 grade II for males and 2 grade I for females.

Nineteen individuals (see Fig. 1) experienced early-onset SRs (occurred within the first 30 minutes after SCIT administration) and 18 SRs were delayed-onset (occurred later than 30 minutes after SCIT administration). The more severe SRs were delayed reactions (grade III and IV). However, all affected individuals responded to therapy without sequelae.

All grade I SRs were effectively treated without epinephrine administration, whereas 58% of the grade II, and 100% of both the grade III and grade IV reactions were administered intramuscular epinephrine. When epinephrine use was examined in conjunction with the onset of the SR, epinephrine was used in 69% of early-onset grade II reactions, and 25% of

delayed-onset grade II reactions. Additional therapy included: the use of diphenhydramine by 22 patients, long-acting antihistamines were used by an additional 10 patients, and systemic steroids were administered to 6 patients. All patients were evaluated in their primary care office and/or an ER.

Discussion

To the best of our knowledge, this is the largest study reporting the safety outcome of a self-administered SCIT protocol for a patient cohort consisting of tens of thousands of individuals. The UAS SR rates are significantly lower than those promulgated for traditional in-office IT protocols ($p < 0.0001$).[2, 14, 22, 27–31] No grade V anaphylactic reactions occurred in over 2 million home-administered injections. In contrast, a review by Bernstein et al.[20] of SRs to SCIT approximated a fatality rate of 3.4 deaths per year and of 1 death per 2.5 million SCIT injections administered for the 12-year period studied. Overall, this study documented 41 reported fatal IT reactions and 273 near fatal reactions.[20] In a large retrospective analysis reported by Ragusa and Massolo, the incidence and characteristics of nonfatal SCIT-induced SRs over a 20-year period (1981 to 2000), were reported.[28] SRs occurred in 5.2% of patients and 0.06% of injections during the first 10 years and 1.08% of patients and 0.01% of injections during the latter 10-year period studied.[28] More recently, Phillips et al.[29] reported a SR rate of 4% in 773 patients who underwent 28,000 SCIT injections. Others have reported SR rates of 14% for traditional IT protocols and rates as high as 36% for more rapid cluster or rush IT regimens.[2, 14, 30]

Several studies have demonstrated the safety of SCIT in the pediatric population.[27, 31] Specifically, SCIT-associated SR rates of up to 4.6% per injection and 3.7% per patient were recently reported.[31] The current study demonstrates safety in one of the largest pediatric SCIT populations studied to date. The pediatric patient SR rate per patient was 0.19% and per injection was only 0.002%. These low pediatric SR rates are significantly below the rates of previous reports ($p < 0.0001$).[31]

Of note, the results of most of the above referenced IT reviews were based upon voluntary surveillance surveys acquired from a variable number of medical practices.[11, 12, 14, 20–22,28] In addition, the specificity and completeness of surveys also varied.[11, 20–22] In contrast, the data acquired in the current study was from sources with well-established lines of communication that fostered the acquisition of reliable information. Furthermore, this study included monthly clinic-based reviews of all local reactions and SRs when patients returned for their dose-logbook examination and unit-dose vial pickup (see Patients and Methods). Thus, we believe the completeness and accuracy of reliable SR-related information is improved under these circumstances.

Self-administered SCIT was originally considered within the spectrum of standard practice.[10] The IT practice parameters criticism of self-administered SCIT is a reiteration of the 1994 AAAI position statement.[2,10] Based upon the results of Lockey et al.[11] and the 1986 UK CSM Update, self-administration of SCIT fell out of favor.[10–12] In the former study, 24 IT-related fatalities were documented prior to 1973 through 1984.[11] Only 1 of the 24 documented fatalities occurred during home-administration or self-administration. This

patient was an asthmatic with significant allergen sensitivity; however, asthma severity, control, and the availability or use of epinephrine were unknown. These 24 reported fatalities were associated with: asthma or chronic obstructive pulmonary disease of unspecified severity and control, cardiovascular disease, persistent chest pain, significant allergen sensitivity, use of beta adrenergic receptor antagonists and respiratory distress at the time of SCIT administration. Furthermore, 8 fatalities did not administer or experienced errors in the administration of epinephrine for anaphylaxis. Also, 21% were a consequence of IT dosing errors. Needless to say, uncontrolled asthma, significant cardiovascular disorders, use of beta adrenergic receptor antagonists, the lack of available epinephrine, and high degrees of allergen sensitization are clinical issues in which IT would not currently be prescribed or administered.[2,21] The other evidence cited in the AAAI position statement was the CSM Update, which documented SCIT-associated fatalities from 1957 to 1979 in the United Kingdom.[12] However, minimal case-related specifics were provided. Salient information such as the availability of epinephrine or the control status of affected asthmatics was not discussed or was unknown and thus somewhat devalues the 1994 AAAI position statement and subsequently promulgated recommendations.

The IT practice parameter caveats pertaining to self-administered SCIT are consistent with classification of evidence category IV and the strength of these recommendations is level D, suggesting not the strongest evidence to support their recommendations.[32] In addition, recent studies have demonstrated improved safety outcomes.[33] There has been 1 reported office-based SCIT fatality since 2008.[33] This unfortunate fatality may have been a consequence of several factors, including a possible high level of allergen sensitivity. In contrast, during this period, there have been no deaths reported for those on self-administered regimens. This safety improvement follows the promulgation of the 2007 NHLBI Asthma guidelines, which have fostered more careful asthma assessment and therapy targeted to disease classification, control, and severity.[26] Of note, since 2009 to the beginning of 2014, over 90,000 patients have received greater than 10 million SCIT injections in accordance with the UAS protocol without the occurrence of death.

More recent reports by Reid et al.[21] and Bernstein et al.,[20] respectively, documented 1 of 17 and 2 of 41 IT fatalities occurring at home. Factors as specified in previous two paragraphs, played a role in the fatalities at medical facilities.[20, 21] Specific issues of asthma control, lack of available epinephrine and recurrent previous anaphylactic episodes directly impacted the fatal outcome of the 3 patients using home-based SCIT.[20, 21] Evident in both reports, as also evident in the previously discussed reports, was the prescribing of SCIT for “high-risk” individuals mostly treated at medical offices.[11, 12, 14, 22, 28]

In contrast, other reviews and studies have reported the safety of regimens established for self-administered IT.[15, 16, 34, 35] The distinction between the outcome of the former and latter reports is related to the selection of patients.

The selection of a low-risk patient population is a common finding in clinical studies and reviews that have demonstrated safe outcomes. This conclusion is further corroborated by noting the results of a large, prospective, self-administered SCIT study in which approximately 636,000 patient encounters and 1,144,000 allergy injections were studied.[35]

The authors suggest that the low reaction rates, infrequent occurrence of serious reactions, and lack of deaths observed in the study were explained by the low-risk patient population treated. The authors further concluded that home-based IT was found to be safe.[35] Of note, 30.5% of otolaryngic allergists practice home-based SCIT during the maintenance phase and 12.9% prescribe self-administered SCIT starting during the buildup phase according to an American Academy of Otolaryngic Allergy Morbidity and Mortality Survey.[36] The survey results demonstrated an exceedingly low (0.3%) SR rate. The authors concluded that home-based SCIT is a safe treatment option in low-risk patients.[36] In addition, a survey of allergists, members of the American Academy of Allergy, Asthma, and Immunology, demonstrated that, "Overall, 16% of respondents allow some home immunotherapy …." This element of the survey demonstrates that a proportion of allergists allow patients to participate in the out-of-office self-administration of SCIT.[37] Furthermore, other allergists have also found home-based SCIT to be safe.[15, 16, 34] One of these allergists demonstrated the safety of home-based SCIT in which over 2 million injections were self-administered.[34] In summary, a preselection of low-risk IT patients is a common factor in studies reporting low SR rates without associated fatalities.

A few sources have previously criticized specific studies in which the formulated IT was suspected to use low concentrations of extracts.[38] This criticism has been effectively addressed by Cook and Farias.[13] The UAS protocols encompass allergen concentrations consistent with the recommendations of the IT practice parameters (Table 2) and have equivalent efficacy.[39]

Historically, a higher proportion of SRs have been reported to occur during the buildup phase.[2, 9, 14, 21, 33, 40] Some recommendations for otolaryngic allergists specify initiating a self-administered protocol once patients achieve maintenance level IT.[14] Wells[15] and Falliers[16] also initiated self-administered SCIT during the maintenance phase. Alternatively, of note, the rate of dose increase during the buildup phase is considered a prominent cause of induced SRs.[9] Thus, several reports have recommended a slow incremental concentration increase or the use of moderate doses during the IT buildup phase as a means of decreasing the frequency of systemic reactions.[14, 40, 41] In accord with these recommendations, more moderate dosing during the buildup phase of cluster SCIT has recently been suggested to diminish the high occurrence of SRs.[33]

European IT practices have traditionally used aluminum adjuvants and more recently other depot adjuvants such as tyrosine for allergoid SCIT.[42–44] The use of these depot adjuvants results in a slower release of the allergoid and has been associated with fewer SRs.[42–44] The increased safety associated with this slower release, in principle parallels the use of a slower buildup phase.

Consistent with the aforementioned recommendations and concepts, the UAS protocol uses a buildup phase in which maintenance is achieved in 6 months, longer than some promulgated regimens but still consistent with the recent IT practice parameters.[2]

This protocol uses cumulative dosing equivalent to that recommended by the practice parameters as evident in Table 2.[2] The cumulative administered allergen extract dose has

been postulated to be the significant factor in IT efficacy with respect to: IT-associated beneficial immunologic changes; allergenic symptom reduction evident in IT efficacy studies, and the long-term clinical benefits of IT.[1, 23, 45–50]

We hypothesize that this slower buildup phase is both safe and efficacious.[39] This slower buildup phase, in conjunction with the preselection of low-risk individuals, may be key factors in the decreased frequency and severity of SRs evident throughout both IT phases in the current study. To substantiate this concept, further investigation of the potential safety and efficacy of a slower IT buildup phase is warranted.

The safety and efficacy of SLIT immunotherapy is well documented in the literature and is an alternative route of IT administration.[8, 47, 48] Although SLIT is frequently used in Europe, currently only 2 SLIT-based grass tablets and 1 SLIT-based ragweed tablet have been approved by the U.S. Food and Drug Administration (FDA) for use in the United States. It is expected that other allergen extracts will be FDA-approved for SLIT administration in the future.

As summarized above, several studies have demonstrated increased safety outcomes for self-administered SCIT during the IT maintenance phase.[13, 15, 16] In the current study, the patient preselection process (and possibly the slow buildup phase) resulted in a lower frequency and severity of SRs compared to previous reports in both IT phases.[2, 12, 20–23, 28–31]

Of the documented 37 SRs, 35 of the affected patients experienced mild adverse events (WAO grade I or II). Only 2 of the affected adult population experienced more severe adverse events (1 grade III and 1 grade IV). Nineteen individuals (51%) experienced early onset SRs and 18 (49%) of affected individuals experienced late-onset reactions (Fig. 1). These results are consistent with several previous reports,[30, 40, 50, 51] but not all.[20, 21, 28, 35] Also consistent with previous reports,[9] affected female patients outnumbered male patients. In this study, a possible rationale for the higher frequency of affected female patients may be due to the higher mean age (and associated propensity for age-dependent morbidity) and the higher frequency of asthma among our female patients (5/7 asthmatics with SRs). Furthermore, only 1 asthmatic patient presented with respiratory symptoms (mild dyspnea) as part of her SR, which were readily addressed therapeutically. All adverse events were effectively treated without sequelae.

Epinephrine was used by 58% of patients manifesting a grade II reaction and both individual's experiencing grade III and IV reactions. With respect to the individuals with grade II SRs who did not use epinephrine, none met the criteria for anaphylaxis.[52] This is consistent with recent recommendations of the UK's Working Group of the Resuscitation Council.[53] Also consistent with these findings, Epstein et al.[22] reported significant percentages of patients with early-onset and delayed-onset mild and moderate SRs that did not receive either office-administered or self-administered epinephrine. In addition, Winther et al.[51] reported that only 2% of nonanaphylactic SRs were treated with epinephrine.

Conclusion

Only 2% to 6% of patients that would benefit from IT undergo therapy.[54, 55] We believe that a carefully implemented self-administered SCIT regimen for low-risk patients during both the buildup and maintenance phases would be clinically safe and efficacious, and would expand the size of the patient pool currently benefitting from IT.[39]

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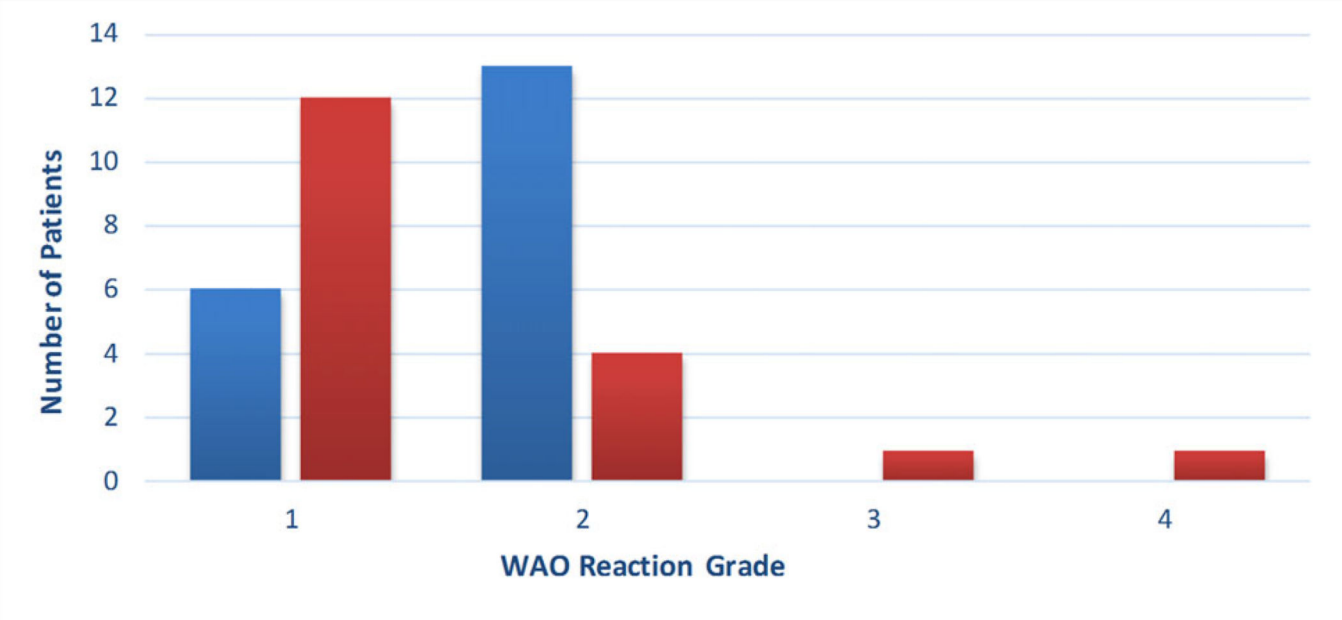

FIGURE 1.

Systemic reactions: grading and early vs late onset. The blue bars represent early onset systemic reactions (≤30 minutes post-SCIT) and the red bars represent late onset systemic reactions (>30 minutes post-SCIT). SCIT = subcutaneous immunotherapy.

TABLE 1

World Allergy Organization SCIT SR Grading System*

Grade I
Cutaneous
Generalized pruritus, urticaria, flushing, or sensation of heat or warmth OR Angioedema (not laryngeal, tongue or uvular)
Upper respiratory
Rhinitis OR Throat-clearing OR Cough perceived to originate in the upper airway, not the lung, larynx, or trachea
Conjunctival
Erythema, pruritus, or tearing
Other
Nausea, metallic taste, or headache
Grade II
Lower respiratory
Asthma: cough, wheezing, shortness of breath (<40% PEF or FEV_1 drop, responding to an inhaled bronchodilator)
Gastrointestinal
Abdominal cramps, vomiting, or diarrhea
Other
Uterine cramps, feeling of impending doom
Grade III
Lower respiratory
Asthma (≥40% PEF or FEV_1 drop, NOT responding to an inhaled bronchodilator)
Upper respiratory
Laryngeal, uvula, or tongue edema with or without stridor
Other
Feeling of impending doom
Grade IV
Lower or upper respiratory
Respiratory failure with or without loss of consciousness
Cardiovascular
Hypotension with or without loss of consciousness
Other
Feeling of impending doom
Grade V
Death

*Adapted from Cox et al.[17]

FEV_1 = forced expiratory volume in 1 second; PEF = peak expiratory flow; SCIT = subcutaneous immunotherapy; SR = systemic reaction.

TABLE 2

Comparison of UAS vs practice parameter's immunotherapy dosing

Allergen extract	Extract concentration	UAS dose per year	Practice parameter dose range per year[a]
Dust mite (mix)	5000 AU/mL (*D. farinae*) + 5000 AU/mL (*D. pteronyssinus*)	8320 AU	6028–24,113 AU
Bermuda grass	10,000 BAU/mL	4160 BAU	3617–18,085 BAU
Standard grass (eg, Timothy grass)	100,000 BAU/mL	20,800 BAU	12,057–48,226 BAU
Short ragweed	100,000 AU/mL short ragweed	18,533 AU	12,057–48,226 BAU

[a]The practice parameter cumulative dose range was calculated by using the exemplified immunotherapy protocol specified in Cox et al.[2]

AU = allergy unit; BAU = bioequivalent allergy unit; UAS = United Allergy Services.