Original Article

Adherence With Allergen Immunotherapy Labeling Guidelines

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What is already known about this topic? There are exceptionally limited data that assessed prescribers' adherence to allergen immunotherapy labeling guidelines.

What does this article add to our knowledge? This study highlights poor adherence to allergen immunotherapy extract vials labeling guidelines and notes this as a potential function of the number of years in practice.

How does this study impact current management guidelines? This study highlights the potential for adverse events that could result from nonadherence to allergen immunotherapy extract vial labeling guidelines and raises questions about reasons of nonadherence and ways to best implement practice guidelines.

BACKGROUND: Little is known about the adherence rate to allergen immunotherapy (AIT) labeling guidelines.
OBJECTIVE: To assess adherence to labeling guidelines of AIT Practice Parameter 2011 at University of Michigan Health Service.
METHODS: AIT vials of 320 patients who received their care at the University of Michigan Health Service were reviewed. Data collected looked at patient identifiers (PI), concentrations in volume/volume (v/v) format, color coding, allergen content, expiration date and instructions about AIT dosing, and systemic reaction treatment. Data were analyzed by using χ^2 test and the Fisher exact test and logistic regression.
RESULTS: Of 238 non-university formulated labels, 65% had 2 PIs, 62% had a v/v concentration, 41% had color coding, 71% had the content listed, and 100% had a recorded expiration date. Only 21% had all 5 recommended components. All 82 University vials had 5 components. Labels with 2 PIs were more likely to have a v/v concentration with its corresponding color coding (odds ratio [OR] 3.84 [95% CI, 1.9-7.7]; $P < .001$). Labels that specified the extract's content were more likely to be color coded or to have a v/v concentration listed (OR 6.3 [95% CI, 3.4-11.8]; $P < .001$). For all AIT vials, complete labels were significantly more likely to have a clear buildup schedule (OR 9.6 [95% CI, 4.2-23.2]; $P < .001$), dosing adjustment after a missed dose (OR 8.2 [95% CI, 3.4-19.8]; $P < .001$) or after a reaction (OR 13.7 [95% CI, 7.8-2.1]; $P < .001$), and clear systemic reaction treatment instructions (OR 9.7 [95% CI, 7.8-24.1]; $P < .001$).
CONCLUSION: Fewer than 25% of the nonuniversity prescribers adhered to AIT practice parameters 5 years after publication. Recording 2 PIs, the v/v concentration, or the color coding increased the likelihood of having a complete label. Complete label contents were associated with clear instructions about AIT dosing and reaction treatment and/or dose adjustments. © 2014 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2015;3:250-5)

Key words: *Allergen immunotherapy; Practice parameters; Practice guidelines; Immunotherapy labeling; Allergen extracts; Student health services; Adherence; Health services research*

Allergen immunotherapy (AIT) was first used successfully in 1911 by Noon,[1] who noticed an association between allergic symptoms and the grass pollination season in England. Recent advances in the clinical application of AIT, as recommended by recent practice parameters, have aimed to significantly improve

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Abbreviations used
AIT- Allergen immunotherapy
CC- Color coding
Exp- expiration date
OR- Odds ratio
PI- Patient identifier
UHS- University Health Services Center
UM- University of Michigan
v/v- Concentration in volume/volume

AIT quality and its clinical outcomes,[2-5] AIT clinical outcomes require the provision of high quality and safe AIT extract preparation and labeling. There has been an iterative process in terms of expanding labeling guidelines during the past 11 years and now 3 sets of published AIT guidelines exist,[2-5] most recently the third AIT practice parameter update published in 2011.[5] Additional up-to-date references are available for the AIT prescriber and the preparers of AIT extracts, in addition to the practice parameters, including allergen extract manufacturer preparation manuals: the Allergen Immunotherapy Extract Preparation Manual, and the United Sates Pharmacopeia's General Chapter 797 (USP 797).[6-11]

The guidelines recommends that all extract vials label should contain 2 or more patient identifiers (PI),[2-5] the expiration date or beyond use date,[2-5] abbreviations or names of allergen content, or a link to a document that lists specific allergen content.[2-5] Labels also should include the concentration of each vial listed in a volume-to-volume (v/v) format, with 1:1 indicating the maintenance concentrate. During the buildup phase of immunotherapy, 4 (and, in some instances, 5) dilutions of the patient's maintenance concentrate are needed. The guidelines recommends using a color-coding system with a red cap that indicates the 1:1 v/v concentrate, yellow for the 1:10 v/v, blue for the 1:100 v/v, green for 1:1000 v/v, and silver for the 1:10,000 v/v dilution (if a fifth dilution is necessary).[2-5] It also is permissible, per the practice parameter recommendations, to use an alphanumeric system that begins at "1" or "A" for the maintenance vials or to list the concentrations of allergens in each vial as alternative labeling methods.[3-5] However, these may be a source of confusion for health care personnel who administer allergy injections, especially if one chose to label in a reverse order with "5" being the concentrate.

The effects of labeling variation, or errors that result from such labeling variation, have not undergone robust prior study. Differences in labeling of AIT extracts can potentially lead to confusion, dosing errors, and increased systemic reactions in nonallergy health care settings (such as a primary care office or college health clinic) who administer but do not prescribe AIT. Such settings handle AIT written by numerous, differing providers (from both allergists and otolaryngologists), which may not be similar in style and have to handle high degrees of labeling disparities that may potentially exist. We thus conducted a study at the University of Michigan (UM) University Health Services Center (UHS) to determine the rate of adherence of non-UM referring prescribers of patients who receive AIT at UHS to the AIT practice parameters guidelines. UHS is a health clinic that services the UM undergraduate and graduate campuses, and provides the opportunity for patients to continue to receive AIT injections from multiple independent providers by using their originally prescribed and mixed serum extract.

METHODS

AIT extract vials labels of all 320 patients who received their care at UHS during the fall of 2013 were reviewed. UHS is a health care clinic located on the central campus of UM. It is accredited by the Accreditation Association for Ambulatory Health Care Inc, a nationally recognized organization. With approximately 80,000 total visits per year and approximately 5000 AIT injection visits per year, UHS is a highly used campus resource. UHS services are available to any enrolled undergraduate and graduate student, faculty and staff, retirees, alumni, and spouses and domestic partners and dependents of these individuals. All AIT extract vials of patients who receive their injections at UHS are stored in alphabetical order in 1 refrigerator. Labels of all 320 available AIT extract vials in the storage refrigerator were checked for the different elements recommended by the third update AIT practice parameter, including the following:

- Two PIs, including the patient's full name, date of birth, and medical record number[2-5]
- Concentration of the vial in v/v format[2-5]
- Allergen content, whether or not abbreviated[2-5]
- Expiration or beyond use date[2-5]
- Color or an alphanumeric coding system that indicates a dilution from the corresponding maintenance concentrate vial[3-5]

Corresponding medical records for each AIT extract vial were screened for the presence of a clear buildup schedule stipulated by the prescriber as well as for the presence of instructions and/or guidance of a clear definition of the signs of a reaction, treatment instructions of a local or systemic reaction, clear instructions about AIT dosing adjustment after a reaction, and clear instructions on dosing adjustments after a missed scheduled dose. All the data were recorded into an Excel spreadsheet (Microsoft Corp, Redmond, Wash) for data keeping. Finally, we performed a Web-based search of each provider listed for the external prescribers by using the American Board of Medical Specialties (www.abms.org, for allergy/immunology and for otolaryngology) and both the American Academy of Allergy, Asthma & Immunology (www.aaaai.org) and the American College of Allergy, Asthma and Immunology (www.acaai.org) Web sites to determine the number of years that each prescribing provider has been in practice. AIT written by UM allergy/immunology faculty were not included for final analysis, per prespecified intent, because all UM allergy/immunology prescribed labels are adherent with the 5 components of the labeling guidelines described in the bullet points above.

The specific outcomes of this study were to determine the extent to which external providers to UHS complied with labeling guidelines and assess factors associated with labeling adherence. The data were uploaded from the Excel spreadsheet into Stata 13 SE (StataCorp, College Station, Tex) and analyzed for descriptive attributes by using frequency analysis as well analyzed for inferential attributes by using the χ^2 and Fisher exact tests, and bivariate logistic regression when appropriate. A predictive model of adherence was formulated by using linear regression and analysis of marginal means. This study was determined to be exempt from ongoing review by the UM Medical School Institutional Review Board under a waiver for quality assurance and/or quality improvement research.

RESULTS

A total of 320 AIT extract vials labels were reviewed, 238 of which were from patients from independent prescribers and 82