

Perceived compliance and barriers to care in sublingual immunotherapy

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Background: For allergy immunotherapy to be effective, patient compliance is critical. However, aqueous sublingual immunotherapy (SLIT) may be considered demanding for patients, requiring strict daily dosing and refilling of medication at regular intervals. In this study we sought to determine how patients perceive their own compliance with SLIT and identify barriers that may hinder compliance.

Methods: Using a retrospective review, 46 patients currently undergoing aqueous SLIT were identified to have less-than-excellent compliance based on frequency of clinic visits for SLIT refills. Twenty-eight of these patients completed a phone survey regarding symptom improvement, compliance, and barriers to care. In addition, 56 patients who withdrew from therapy before completion were polled about barriers to adherence.

Results: Of the 28 patients participating in the initial phone survey, 24 (86%) reported subjective improvement in symptoms on SLIT, despite less-than-excellent compliance. Nineteen (68%) of these patients perceived their own compliance to be excellent. Eighteen patients (65%) reported the inconvenience of scheduling and attending clinic

appointments to be the main reason for noncompliance. The most common reasons for withdrawal from therapy were cost (27%), lack of effectiveness (25%), and difficulty with compliance (14%).

Conclusion: The majority of aqueous SLIT patients perceived their compliance to be excellent, although, based on a previous study, these patients did not reach excellent compliance benchmarks. Inconvenience of clinic visits and cost of therapy were found to be the most common barriers to care. Despite what providers perceived as less-than-excellent compliance, 82% of patients reported symptom improvement with SLIT. © 2017 ARS-AAOA, LLC.

Key Words:

allergic rhinitis; allergy; compliance; hypersensitivity; immunotherapy; sublingual immunotherapy; survey

How to Cite this Article:

Kumar MS, Oh MS, Leader B, et al. Perceived compliance and barriers to care in sublingual immunotherapy. *Int Forum Allergy Rhinol.* 2017;7:525-529.

Sublingual immunotherapy (SLIT) is a form of allergen immunotherapy that has been demonstrated in numerous clinical trials to be both safe and efficacious.¹ Therapy requires administration of allergen extracts in prescribed doses and at regular intervals, and thus compliance may be

challenging for many patients. Previous studies have shown compliance rates with SLIT, defined as consistent administration of scheduled doses, to range from 72% to 79% in adults, with rates higher in children.²⁻⁴ In addition, compliance with SLIT appears to decrease over time, which is a concern for a therapy that requires at least 3 years of adherence to be effective.^{1,4}

Although some studies have investigated rates of compliance with SLIT, few have probed into the specific reasons for patient noncompliance. Identifying barriers to care and reasons for noncompliance is essential in maximizing the efficacy of a self-administered therapy such as SLIT. The purpose of this study was to assess patients' perception of their own compliance with SLIT and to identify barriers that may hinder compliance.

Patients and methods

Approval for this study was obtained from the institutional review board of Emory University. A retrospective chart

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Potential conflict of interest: S.K.W.: Medtronic and Merck, consultant; Genentech, research support; Greer Laboratories, Scientific Advisory Board. Presented at the AAOA Annual Scientific Meeting on September 16, 2016 in San Diego, CA.

Received: 26 August 2016; Revised: 9 November 2016; Accepted: 13 December 2016

DOI: 10.1002/alar.21920

View this article online at wileyonlinelibrary.com.

review was performed to identify patients who were undergoing SLIT as of July 21, 2014 in the Department of Otolaryngology-Head and Neck Surgery at Emory University. In addition, patients who began SLIT between September 1, 2007, and July 21, 2014, but did not complete the full course of therapy, were identified. Patients <18 of age were excluded from the study, because factors outside of the patient's direct control may affect their compliance (i.e. parental factors).

Aqueous SLIT in our practice is performed with drops that are mixed in-house for each patient with an individualized prescription based on allergy test results correlated with patient symptoms. Patients must return every 90 days to meet with either a provider or a nurse for vial refills. Data collected for each patient identified by chart review included length of therapy and average number of days between SLIT vial refills. Based on these data, patients were stratified by their level of compliance with therapy, as previously described by Leader et al.⁵ Compliance was considered to be excellent if the average number of days between visits was within a 10-day window of 90 days; good if 11 to 15 days; fair if 16 to 20 days; and poor if ≥ 25 days. Any patient with a compliance level other than excellent was considered noncompliant for the purposes of this study. Noncompliant patients were contacted by phone, and verbal consent was obtained for this study. Each of these patients was administered a survey regarding symptom improvement, therapy compliance, and barriers to compliance (Table 1). Patients who withdrew from therapy altogether were contacted in the same manner and prompted for their reason(s) for discontinuation. Responses to open-ended questions were later categorized based on similarities in content. Descriptive statistics for these responses were calculated.

Results

Forty-six noncompliant SLIT patients were identified using the definition stated previously, 28 of whom successfully completed the phone survey. This included 16 men (57%) and 12 women (43%) ranging from 25 to 68 years of age. Mean age of respondents was 41 years. Fifteen patients (53%) reported substantial improvement in symptoms since beginning SLIT, 8 (28%) a moderate improvement, 1 (4%) a mild improvement, and 4 (14%) reported no improvement. Sixteen patients (57%) felt that they came into the office for refills within 7 days of the 90-day mark after their last refill, 4 (14%) felt they are off by up to 2 weeks, 2 (7%) felt they are off by up to 3 weeks, and 5 (18%) reported being off by 4 or more weeks (1 declined to respond). Nine patients (32%) reported running out of drops before 90 days, 7 (25%) reported the vials lasted >90 days, 9 (32%) reported running out of drops on time for their scheduled refill, and 3 (11%) were unsure. Fourteen patients (50%) claimed never missing doses; 9 (32%) claimed missing no more than 1 dose per week;

TABLE 1. Compliance questionnaire. Phone questionnaire that was administered to patients identified as noncompliant. All questions were multiple choice except for question 5, which was open-ended

1. Have you noticed an improvement in your allergy symptoms since beginning treatment? If so, how much?
(a) No
(b) Yes; mild improvement
(c) Yes; moderate improvement
(d) Yes; substantial improvement
2. In the last year, how close to every 90 days are you refilling your drops?
(a) Within 1 week
(b) Within 2 weeks
(c) Within 3 weeks
(d) Within 4 or more weeks
3. When are you running out of drops?
(a) Sooner than 90 days
(b) About 90 days
(c) Later than 90 days
4. How many times per week do you forget to take your drops?
(a) Never
(b) No more than once a week
(c) Two or three times per week
(d) More than three times per week
5. What is the most frequent reason you are unable to pick up your drops at three months?

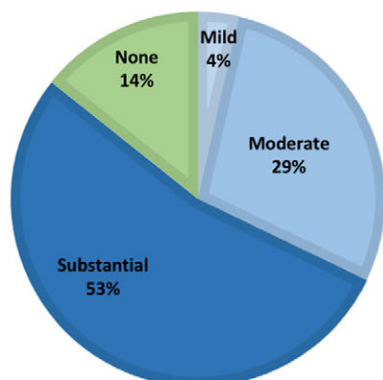
and 5 (18%) claimed missing, on average, 2 doses per week. When asked what is the greatest barrier to coming to the office for refills, 11 patients (39%) reported that the inconvenience of scheduling and attending an office visit was the most substantial barrier, 7 (28%) cited having to take time off from work, 4 (14%) cited travel time to clinic, 1 (4%) cited financial reasons, and 5 (18%) denied any barriers. These results are summarized in Figure 1.

Chart review also identified 116 patients who withdrew from therapy prior to completion, 56 of whom were reached by phone and completed a phone interview for this study. This group of 56 patients included 23 men (41%) and 33 women (59%), ranging in age from 18 to 81 years. Mean age of respondents in this group was 42 years. Fifteen patients (27%) reported discontinuing due to the cost of therapy. Fourteen (25%) found the therapy to be ineffective. Eight (14%) found compliance with therapy to be too difficult. Five (9%) could not tolerate the side effects. Five (9%) relocated and did not establish care with a new provider. Five (9%) became pregnant and stopped therapy. Four (7%) cited other patient-specific reasons. These data are presented in Figure 2.

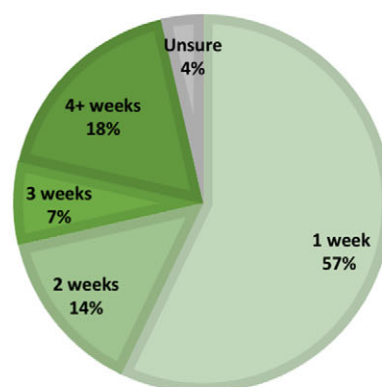
Discussion

SLIT is a safe and effective therapy for the treatment of respiratory allergies. As with any therapy, however, its effectiveness is dependent upon the patient's compliance with therapy as scheduled. The at-home administration of

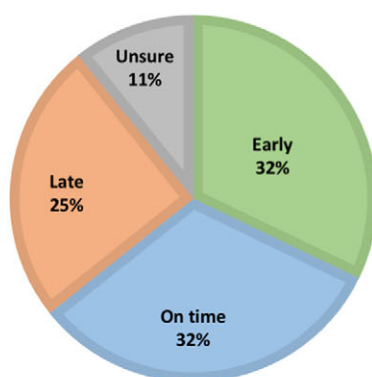
A. Have you noticed an improvement in allergy symptoms since beginning treatment?



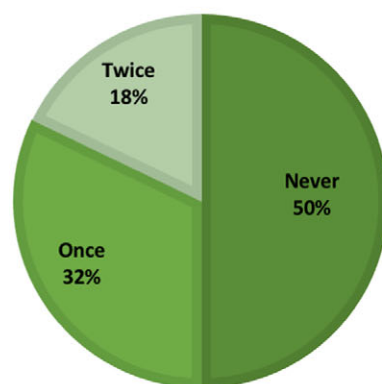
B. How close to every 90 days are you refilling your drops?



C. When are you running out of drops in your vial?



D. How many times per week do you forget doses?



E. What is the most frequent reason you cannot pick up your drops?

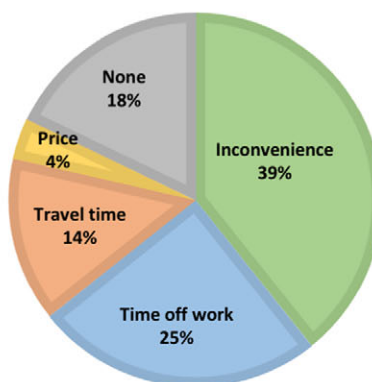


FIGURE 1. Response to compliance surveys showing the results of the phone questionnaire presented in Table 1. Twenty-eight patients identified as noncompliant with the aqueous SLIT regimen completed the questionnaire. SLIT = sublingual immunotherapy.

SLIT theoretically provides an advantage to patients over the traditional in-office administration of subcutaneous immunotherapy (SCIT), which requires frequent visits to a provider for injections. However, we recently reported

that compliance with SCIT is higher than compliance with SLIT among patients in our practice.⁵

Identification of barriers to compliance and efforts to minimize these barriers should theoretically increase

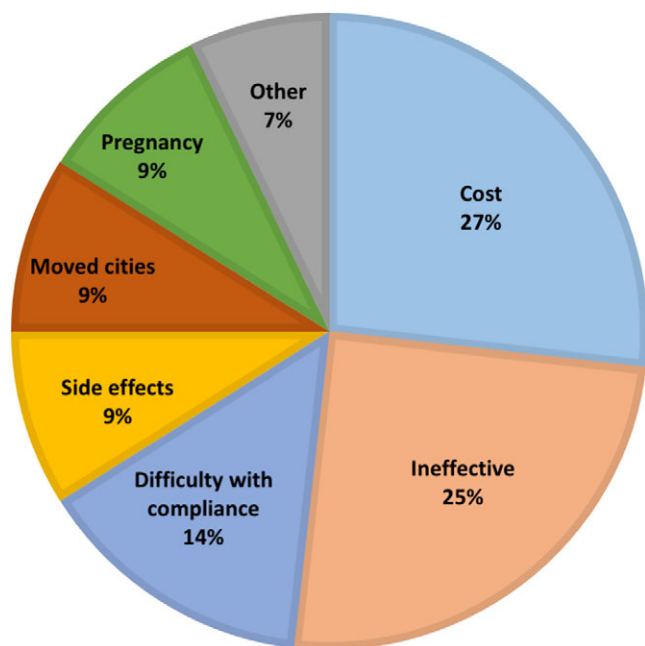


FIGURE 2. Reasons for withdrawal from therapy. The 56 patients who prematurely withdrew from therapy provided their primary reason for withdrawal.

compliance and therefore increase effectiveness of therapy. Although many studies have focused on SLIT adherence rate (the inverse of withdrawal rate), few have investigated the compliance rate for those patients currently undergoing therapy. Even fewer have addressed the specific reasons for noncompliance. A retrospective observational study by Malet et al addressed the compliance rate and reasons for noncompliance in 380 subjects undergoing SLIT for house dust mite allergy. They found that 79.7% of patients were compliant with therapy over a 12-month period, with compliance defined as taking $\geq 80\%$ of the prescribed medication. Fifty-three percent of adult subjects cited “forgetting to take doses” as their main reason for noncompliance. Thirty-four percent cited “complexity and duration of treatment,” 28% cited “difficulty in taking medication according to schedule,” and 21% cited “high cost of treatment.”²

We previously reported an “excellent” or “good” compliance rate of 66% for patients undergoing SLIT in our practice, using the aforementioned definitions of compliance.⁵ In the current study, reasons for noncompliance were due almost entirely to factors related to coming to the clinic. Inconvenience, taking time off from work, and travel time accounted for 78% of responses. Although not a part of the questionnaire administered, many patients expressed the desire for drops to be available for pickup without having to see a provider or being able to pick them up from a local pharmacy. Although we, as providers, view SLIT as an active therapy personalized to each patient, similar to chemotherapy or radiation therapy, many patients seemed to perceive it similarly to other prescribed medications. Certain respondents expressed frustration and lack of

understanding regarding devoting extra time and effort toward acquiring this “medicine” compared with their other medicines. Patients’ perceptions about therapy were not explicitly measured in this study, and thus further research is required to assess how patients perceive SLIT in comparison to therapies for other medical conditions. However, our study does suggest that adjustment of patients’ perceptions and expectations of SLIT may be required to increase willingness to comply with therapy.

It is important to note that comparing results from various studies on SLIT compliance may be difficult, as experimental design between studies varies considerably. First, there is no consistent threshold for what constitutes compliance, and each provider or investigator may define it differently. In addition, there are many ways to assess compliance. Previously reported methods of measuring compliance have included counting remaining medication,^{2,6} assessing frequency of visits for refills,⁷ and tracking regular dose intake.³ As patients in the current study were identified via retrospective review, the method of assessing timing of visits was used for patient selection. This method, although easy to track via chart review, does not assess how often patients are missing doses versus administering an inadequate volume of extract per dose.

Although providers can attempt to minimize barriers to care for their patients, ultimately patients’ compliance with therapy will not change if they are not made aware of their noncompliance. In previous studies regarding noncompliance, patients were asked why they missed doses. In the current study, we asked patients who were defined as noncompliant to assess their own compliance with therapy. Of known noncompliant patients, 50% claimed never to miss doses, and 32% claimed to be compliant with picking up refills at regular 90-day intervals. These findings suggest that additional patient education may be required to ensure that patients understand the requirements of therapy and increase awareness of their own noncompliance.

As with any medical therapy, the goal of increasing compliance is to increase therapy effectiveness and thus quality of life. A recent study by Lemberg et al demonstrated that SLIT does have a positive effect on multiple quality-of-life measures in patients with allergic rhinitis.⁸ In the current study, despite noncompliance, 53% of patients reported a substantial improvement in symptoms since beginning therapy, and another 33% reported either a mild or moderate improvement. It is premature to draw conclusions from these results, and the possibility that this may represent the placebo effect of immunotherapy rather than the true efficacy of therapy at low compliance levels should not be discounted. Further research comparing dose compliance to perceived symptom improvement in a placebo-controlled setting may shed light on whether or not strict compliance is required to increase quality of life for these patients.

In identifying barriers to care with SLIT, we also contacted patients who had withdrawn from therapy prior to completion to assess their reasons for withdrawal. A 2010 study surveyed 296 Italian allergists regarding why they

think their patients discontinue therapy. The primary reason as perceived by the allergists was lack of effectiveness, followed by inability to tolerate side effects, cost of therapy, and difficulty with compliance.⁹ The results of our survey of former patients mirror these reasons with the exception that cost of therapy was the most common reason for withdrawal, with 27% of patients citing this as their primary motivation for withdrawal. This percentage likely underestimates the role of cost on therapy withdrawal, as many patients who cited lack of adequate effectiveness as their primary reason (25%) also mentioned that the cost-to-benefit ratio was not suitable enough to continue therapy. It is possible that some of these patients may have seen an improvement in their symptoms had they continued therapy to completion, but cost prohibited them from doing so. Unlike some European countries, aqueous SLIT is not covered by insurance companies in the United States, presenting a substantial financial burden to patients undergoing this therapy.⁴ Higher medication costs and low income have repeatedly been shown to correlate negatively

with medication adherence in developed countries.¹⁰ Measures to lower the cost of therapy are likely to be most effective in increasing patient willingness to begin and continue SLIT.

Conclusion

The majority of aqueous SLIT patients perceived their compliance to be excellent even though they did not reach excellent compliance benchmarks from the provider's perspective. Nonetheless, the majority of these patients reported improvement of symptoms despite the less-than-excellent compliance. The inconvenience of clinic visits to refill medication and the high cost of therapy were found to be the most commonly cited barriers to care in our study. Efforts to minimize these factors will likely have a positive effect on patient compliance with SLIT. Further research is needed to determine what level of compliance is required for therapy to be effective from the patients' perspective. 

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