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Determinants of patient compliance with allergen immunotherapy

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Background: Allergen immunotherapy (AIM) has been demonstrated to be safe and effective in the treatment of allergic respiratory disease. Although it requires considerable patient commitment, little attention has been paid to the factors that contribute to patient compliance.

Methods: Patients in a practice based at an urban university hospital, who discontinued AIM, were contacted to determine their reasons for stopping treatment. Results were correlated with demographic and disease data obtained from the patient charts.

Results: Review of practice records identified 217 patients on AIM. One hundred forty-eight had allergic rhinitis (R), 66 had allergic rhinitis and asthma (RA), and 3 had allergic asthma without evidence of rhinitis (A). Seventy-four (50%) of the patients in the R group, 32 (48%) of the patients in the RA group, and three (100%) of those in the A group discontinued treatment. The groups differed in that 55% of the patients in the R group discontinued treatment because of inconvenience, compared with only 22% of the patients in the RA group ($p < 0.01$). By contrast, 25% of the patients in the RA group stopped because they thought that they were "better" with medication, compared with none of the patients in the R group ($p < 0.001$). All of the patients in the RA group who stopped because they were better completed at least the first four-vial treatment series.

Conclusions: Inconvenience is the major contributing factor in noncompliance with AIM. Regulations designed to protect patients from adverse reactions should balance the potential risk of reactions against the benefits of treatment and the effect of more stringent guidelines on patient compliance. (*J ALLERGY CLIN IMMUNOL* 1993;91:734-7.)

Key words: Allergens administration and dosage, asthma, allergic rhinitis, desensitization immunologic adverse effect, hay fever therapy, pollen immunology, asthma therapy, patient compliance

There has been considerable interest in recent years in allergen immunotherapy (AIM) for the treatment of allergic rhinitis and asthma. Particular attention has been paid to the risks associated with allergen im-

Abbreviation used

AIM: Allergen immunotherapy

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munotherapy, and various safety criteria have been proposed to minimize life-threatening complications.¹⁻³ By contrast, no published studies exist addressing the factors that determine patient compliance with immunotherapy prescribed by their physician. These factors have potentially important implications at a time when there is increasing concern about deaths from asthma⁴ as well as increasing evidence that AIM offers an effective additional avenue of treatment for that disorder.⁵⁻⁹

TABLE I. Profile of patients

	R	RA	A
No. of patients on AIM (216)	148	66	2
Total male (%)	55 (37)	21 (32)	—
Total female (%)	93 (63)	45 (68)	2
Mean age	41 yr	44 yr	63 yr
Patients discontinuing AIM (%)	74 (50)	32 (48)	2 (100)

R, Patients with allergic rhinitis; RA, patients with allergic rhinitis and asthma; A, patients with asthma only.

METHODS

Subjects

All patients were initially prescribed treatment by a single practitioner (J.R.C.) in an urban, university hospital-based combined allergy and pulmonary practice. Allergen immunotherapy was recommended to patients who had persisting symptoms but had failed to obtain satisfactory relief from conventional treatment with medication and environmental control. This could reflect either persisting symptoms from their allergic respiratory disease or adequate relief that required multiple medications with unpleasant or intolerable side effects.

Of the patients who discontinued therapy, all of the patients with allergic rhinitis and asthma and 62 of the patients with allergic rhinitis had symptoms for more than 5 years when they initially came for treatment. All but one of the patients with allergic rhinitis had symptoms for at least 3 years, whereas one patient had only 2 years of symptoms. All patients had tried multiple medications, with more than one half of the asthmatic patients having taken systemic steroids for at least some period of time. Virtually all of the patients with allergic rhinitis and asthma had taken inhaled steroids and theophylline. Our practice includes a large number of professional performers, for whom medication may present problems¹⁰; allergen immunotherapy has no adverse effect on the voice.¹¹ Most patients had symptoms for more than one "season" each year, including 83% of the patients with allergic rhinitis and 77% of the patients with allergic rhinitis and asthma who had perennial symptoms.

When a patient elects to undergo a course of AIM, a prescription for a custom vaccine is prepared and placed on a 5 × 7-inch card. Renewals are also noted on the same card. The names of all patients who ordered a new or renewal vaccine from January 1989 to July 1991 were obtained from the card file.

Survey

Patients who had not renewed their vaccine in 6 months or more were contacted by an office nurse (A.P.) who explained that she was doing a research project and then said, "I have noticed that you have not renewed your vaccine in some time. May I ask why?" Information was obtained from patient charts for diagnosis, duration of treatment, age, and sex. Individual answers were grouped to permit analysis into categories, based on their answers. Prompting of patients to obtain additional reasons for stopping treatment

was not done, because we did not want to make patients feel uncomfortable by asking multiple questions about why they had not followed the prescribed course of therapy.

Analysis

Because only three patients were in the group with asthma only, they were omitted from the final analysis. The group with allergic rhinitis and the group with asthma and rhinitis were then compared by Fisher's Exact Test to determine if there were any significant differences between the groups.

Immunotherapy protocol

Patients are required to obtain treatment series injections in a medical facility where a physician is present. In our office patients are expected to wait 20 to 30 minutes after each injection while on an increasing dose and 15 to 20 minutes when on a fixed maintenance dose. Patients who are on maintenance doses are discouraged from home administration of injections. If they inquire about that possibility, they are given a paper discussing the morbidity and mortality rates associated with immunotherapy and the Academy's statement that addressed that issue.³ They are asked to sign a release that indicates home immunotherapy represents an increased risk of a fatal reaction and is not encouraged.

Initial inhalant immunotherapy prescriptions consist of four vials representing a 5.0 ml maintenance vial and three 10-fold dilutions. Six to seven doses of increasing strength are required to complete each dilution vial up to a maximum dose of 0.5 ml. Renewals are prepared as sets of two 5.0 ml vials of identical composition. The concentration is increased if the prior maintenance dose was well tolerated. Injections are given weekly during the first year, every other week in the second year, every third week in the third year, and monthly thereafter. The uncertain benefit of continued treatment is reviewed with the patient during the fourth or fifth year. Most of the patients who stopped treatment on their own did so by the second year, with 46% stopping by the end of the first year of therapy.

Overall compliance

Two hundred seventeen patients were identified (Table I). This included 148 patients with allergic rhinitis, 66 with rhinitis and asthma, and two with asthma only. Approximately one third of each group were men and two thirds were women. The mean age in each group was also similar

TABLE II. Reasons for discontinuing immunotherapy

	Allergic rhinitis (R)	Asthma & rhinitis (RA)	Total
Inconvenient*	41 (55%)	7 (22%)	48 (45%)
"Pessimist"	6 (8%)	3 (9%)	9 (8%)
Other illness	6 (8%)	5 (16%)	11 (10%)
Better w/meds‡	0 (0%)	8 (25%)‡	8 (8%)
No sx/no meds	6 (8%)	2 (6%)	8 (8%)
Status unknown	15 (20%)	7 (22%)	22 (21%)

Inconvenient, Discontinued because it was inconvenient to come for injections; *Pessimist*, patient did not think AIM would be effective;

Other illness, a concurrent illness prevented continuation; *Better w/meds*, Satisfactory control of symptoms that the patient attributed to medication; *No sx/no meds*, without symptoms and on no medications.

Fisher's Exact Test, R versus RA: * $p < 0.01$, † $p < 0.001$.

‡All patients who considered themselves "better with medication" completed at least the initial treatment series of 26 injections.

(patients were in their early forties), reflecting the largely adult nature of this practice. Both patients in the asthma only group discontinued treatment. Approximately one half of the group with allergic rhinitis (50%) and the group with rhinitis and asthma (48%) stopped treatment.

Reasons for discontinuation

Fifty-five percent of the patients with allergic asthma discontinued AIM because of inconvenience, as compared with only 22% of the patients with rhinitis and asthma (Table II). By contrast, 25% of the patients with rhinitis and asthma discontinued treatment because they perceived that they were "better with medication," whereas none of the patients with allergic rhinitis gave that reason for stopping. All of the patients with allergic rhinitis and asthma who stopped AIM because of "improvement with medication" completed the initial treatment series of approximately 30 injections. Both of these differences between the patients with allergic rhinitis and asthma and patients with allergic rhinitis were statistically significant at the $p < 0.01$ level or less. Smaller numbers of patients in each group discontinued AIM because of intercurrent illness, complete control of their symptoms, or doubts that treatment would be effective.

DISCUSSION

Almost one half of the patients who were on AIM discontinued treatment. This is comparable to the results reported by others with a pediatric patient population.¹² Although our patients were virtually all "private patients," some had insurance that covered the total cost of their injections. We did not examine the effect of insurance coverage on compliance. Lower et al.¹² studied a more mixed population. "Paying" patients were more compliant with immunotherapy than those covered by medical assistance, suggesting cost was not a factor. We discuss the cost of treatment with each patient before starting therapy, but it is

certainly possible that some patients were discouraged by this aspect, although they gave a different explanation for stopping.

A significant difference existed in the reasons for discontinuing immunotherapy between our two groups. More than one half of the patients with allergic rhinitis discontinued immunotherapy because of inconvenience. This compared with only 22% of the patients with rhinitis and asthma who cited that reason for stopping. This may reflect the more severe nature of asthma as an illness, making "convenience" a less important factor. AIM is presented in our office to patients with allergic rhinitis as one of a variety of options for treating what is primarily an annoying but not life-threatening illness. Immunotherapy is instituted because a patient thinks at the time that the inconvenience and expense of treatment appears to be less than that represented by their allergic symptoms themselves on pharmacologic treatment. It is not unreasonable to expect that a significant portion of the patients with rhinitis, once they have been coming for weekly injections, and once their symptoms improve as the seasons change, will decide that immunotherapy is no longer "worth it."

By contrast, asthma is treated as a much more serious problem. It may significantly interfere with a patient's daily activities as well as result in life-threatening disease. It is possible that our patients with asthma tend to view this treatment as an important health measure, and so they are less likely to be discouraged by inconvenience.

Twenty-five percent of the patients with asthma discontinued AIM because they perceived they were "better with medication." None of the patients with allergic rhinitis cited this reason. Because manage-

ment is more complex, when patients with asthma come to a specialist who treats that disorder, more pharmacologic options are available, and therefore more opportunity exists to improve their symptoms. Appropriate workup may identify exacerbating factors such as chronic sinusitis, gastroesophageal reflux, or even a pet in the house, where intervention may result in some improvement. Every effort is made to identify and treat such factors before starting AIM. By contrast, our perception is that patients with allergic rhinitis have already been treated aggressively with antihistamines and topical steroids by their primary physicians, providing fewer options to alter pharmacologic treatment.

All of the asthmatic patients who indicated they were improved with medication completed at least the first course of treatment. This consists of four vials, representing a "maintenance" vial and three 10-fold dilutions. The last vial contains 5.0 ml of allergen, with a maximum dose of 0.5 ml. If no significant local reactions occur to prevent proceeding, there are 26 injections to the maintenance dose. If a patient comes only once a week, they are on immunotherapy for more than 6 months before they complete the initial series. It is possible that some of the improvement experienced by the patients with rhinitis and asthma was actually a result of the immunotherapy they received.

CONCLUSION

As a result of several articles that appeared in the past several years, considerable attention has been paid to the risks associated with AIM.^{1, 13-15} Most of these data are retrospective. It is difficult to know the precise incidence of adverse reactions when compared with the huge number of injections given each year throughout the United States.

The Executive Committee of the American Academy of Allergy and Immunology balanced the question of safety requirements for the administration of immunotherapy against the relative risk of reactions and the need for realistic regulations in a statement published in 1986.³ They were unable to reach an agreement and published a paper containing both the "restrictive and flexible position." In a subsequent statement, a unified response was issued related to the waiting period after allergy shots are given.² Our data support the results of their efforts at weighing the risks and benefits of AIM along with the need for realistic guidelines for administration.

Overall, 45% of our patients discontinued immunotherapy because of inconvenience. It seems rea-

sonable to expect that if the waiting period is lengthened further, resuscitation equipment requirements are tightened to make it impossible for primary care providers, student health centers, and similar facilities to administer immunotherapy, and home immunotherapy is prevented, the rate of patients discontinuing treatment because of inconvenience will increase. Ironically, it is those patients who have the most severe asthma who are at the greatest risk of reactions,¹⁴ but they may also benefit the most from treatment.⁹

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