

Allergy symptom response to intradermal testing-based immunotherapy: A retrospective study of clinical practice

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OBJECTIVE: Evaluate the multiple end-organ targets affected by intradermal testing (IDT)-based immunotherapy.

STUDY DESIGN AND SETTING: We conducted a retrospective medical record review of 139 patients, as well as a follow-up questionnaire in a university setting.

RESULTS: Statistically significant differences (*t*-tests, $P < 0.05$) were observed in the prevalence of symptoms after IDT-based immunotherapy for each category (ear, eye, nasal, and throat). When divided into treatment time groups, the reduction was less in the first group (0-6 months therapy), than the subsequent groups (6-24 months and >24 months). The reduction leveled off after 6 months of therapy, with no difference seen between the 6- to 24-month and >24-month groups.

CONCLUSIONS: IDT-based immunotherapy has a broad response on otolaryngic allergy symptoms that appears to be consistent over time.

SIGNIFICANCE: IDT-based immunotherapy is an effective form of treatment for allergy-induced diseases of the head and neck. (Otolaryngol Head Neck Surg 2004;131:220-4.)

Allergy and related symptoms of the head and neck are estimated to affect more than 15% of the American population, resulting in billions of dollars in health care costs each year.^{1,2} With the head and neck region being the portal of entry for inhalant and food allergens, it is not surprising that some of the most common allergy-induced diseases occur in this region. For the practicing otolaryngologist, this means that patients with allergy complaints are encountered daily with a wide range of presenting symptoms including sinonasal, otologic, ophthalmic, and laryngeal concerns.

Once allergy has been defined clinically, treatment in the form of allergen avoidance, pharmacotherapy, or

intradermal testing (IDT)-based immunotherapy is initiated. The American Academy of Otolaryngic Allergy has published a standardized protocol for performing IDT testing.³ Ideally, the clinician would be able to objectively follow therapeutic responses. Unfortunately, an objective measurement of allergy therapy effectiveness and IDT-based immunotherapy is currently not available to the clinical otolaryngologist. Repeat in vitro testing or skin testing have not been shown to correlate with symptomatic relief of symptoms. At this point, a patient's perception of their disease is clinically the best way to follow the allergic patient treated with immunotherapy.

Recently, there has been interest in developing questionnaires to follow therapeutic outcomes and quality-of-life issues related to the allergic disease process.^{2,4-7} When adapted to allergy in an otolaryngology practice, current validated questionnaires focus mainly on rhinitis and nasal symptoms. Examples of such questionnaires include the Rhinosinusitis Disability and the Sino-Nasal Outcome Tests, which have limited inquiry about otologic-, laryngeal-, or ophthalmic-related allergy symptoms.

The aim of the current study was to evaluate the multiple end-organ targets affected by IDT-based immunotherapy. A cohort of patients treated in an otolaryngic allergy clinic were studied to define the prevalent symptoms (nasal, otologic, ophthalmic, and laryngeal) prior to and during immunotherapy. Changes in symptomatic responses were used to support the benefits of IDT-based immunotherapy.

METHODS

The current study was approved by the University of Kansas Medical Center Institutional Review Board as a class 4 exemption.

Subjects

All patients were actively followed in the allergy clinic of the Department of Otolaryngology-Head and Neck Surgery at the University of Kansas Medical Center. A total of 139 patients were included in this study. All patients received immunotherapy after having a specific set of allergens identified by IDT testing. Only patients who had completed an initial allergy symptom questionnaire prior to their first appointment were included in this study. Patients who were no longer being followed or who had not filled out an initial questionnaire were not in-

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Table 1. Allergy history follow-up form

Date: _____ Age: _____

Name: _____

Do you feel you have had improvement since your initial visit? Y N

What do you feel is your main problem now? _____

Have you had any complications from allergy shots? Y N

What were they? _____

Did you have to use the epi-pen? Y N

What medications are you on now? _____

Have you had any surgeries since initiating therapy? Y N

What were they? _____

How many sinus infections have you had in the last year? _____

How many times did you have to take antibiotics for the sinus infections? _____

Has your sense of smell improved Y N Has your taste improved? Y N

Are you smoking? Y N How much? 1 2 3 packs/day

Circle all symptoms you have experienced *IN THE LAST MONTH*

Nose itching, sneezing, blocking, snoring, discharge, postnasal drip, inability to breath, redness, frequent colds, polyps, sinus trouble

Eyes itching outer corner, itching inner corner, puffiness of lids, blurring of vision, excessive tearing, dark circles under eyes

Ears itching, itching deep in ears, frequent infections, ringing, dizziness, popping, fullness, pressure, hearing loss, drainage

Throat frequent sore throats, itching of palate or back of throat, difficulty swallowing, lump sensation, laryngitis, burning sensation when drinking juice or coffee, need to clear mucous in the morning, mouth ulcers, swelling of lips, swelling of tongue, scratchy or burning sensation

cluded. The majority of patients (93%) had been treated with immunotherapy for more than 6 months.

Materials

At the time of initial evaluation, prior to being seen in the allergy clinic, all patients were asked to complete a thorough allergy history packet. A section of symptoms from 4 categories (nose, eyes, ears, throat) was included. Patients were asked to identify symptoms that they had experienced in the last month by circling the symptoms listed on the history form. A follow-up form was given during IDT-based immunotherapy that included demographic data, questions about complications, medications, surgeries, and infections since initiating immunotherapy as well as the same list of symptoms found in their initial history packet presented in a similar fashion during the course of their therapy (Table 1). Symptoms were not graded. No questions pertaining to quality of life were specifically addressed.

Procedures

All patients seen in follow-up in the allergy clinic were asked to complete the single-page questionnaire while in the waiting room prior to being seen by the physician. The data were collected by the clinic nurse and placed into the patient's allergy clinic chart. After 6 months of data collection, patient charts were reviewed. Data were collected from patients meeting the inclusion criteria as defined above. Total number of symptoms prior to immunotherapy in each category (ears, nose, eyes, throat), as well as the presence of individual symptoms were evaluated and compared with those during treatment.

Statistical Analysis

To statistically evaluate whether an individual symptom (i.e., "sneezing") was effectively treated via immunotherapy, the McNemar change test was performed (2-tailed). This allowed each subject to be used as his/her own control. To statistically evaluate whether the number of symptoms reported in each of the 4 major categories (ears, nose, eyes, throat) improved with immunotherapy, paired t-tests were performed (2-tailed).

RESULTS

The mean age of the patients included in this study was 48 years (range, 10-82 years), and 66% were female. Of the patients, 7% had been treated with IDT-based immunotherapy for less than 6 months, 40% had been treated for 6 months to 2 years, and 53% had been treated for more than 2 years. The reported patient-viewed complication rate was less than 10%, the vast majority of which were related to local skin irritation or pain following an injection. There were no serious complications, including anaphylaxis. Of the patients, 34% reported an improvement in taste and 36% reported an improvement in their sense of smell since initiation of immunotherapy.

Of the 139 patients included in the present study, all had some form of nasal complaint at the time of initial evaluation. The most prevalent symptom was general "sinus trouble" with sneezing being the second most prevalent symptom. Table 2 includes the three most prevalent symptoms reported initially in each of the four major categories included in this study. The fol-

TABLE 2. Percent of most prevalent symptoms reported pre and during immunotherapy

Category	Symptom	Pre %	F/U %	McNemar P-value
Nasal	Sinus trouble	87	62	<0.001
	Sneezing	83	60	<0.001
	Post nasal drainage	69	50	<0.05
Ophthalmic	Itching inner corner eye	58	41	<0.001
	Itching outer corner eye	53	38	<0.001
	Puffiness of lids	46	33	<0.001
Otologic	Feeling of fullness	51	36	<0.001
	Itching deep within canal	49	35	<0.001
	Pressure	47	33	<0.001
Laryngeal	Need to clear mucous in a.m.	62	45	<0.01
	Sore throat	48	35	<0.001
	Scratchy/burning throat	32	23	<0.001

low-up percentage of symptoms reported after immunotherapy was initiated is also shown. McNemar change test results revealed that each symptom significantly decreased in prevalence with immunotherapy (*P*-values shown on Table 2).

Figure 1 shows the number of symptoms before and during immunotherapy that were reported for each category (error bars = standard error of the mean). Paired *t*-tests were performed for each category to determine whether changes occurred in the number of symptoms that were reported. Results revealed significantly fewer symptoms were reported after immunotherapy for each category (*P* < 0.001 for ear, eye, nasal, and throat). Interestingly, the proportions of symptoms prior to treatment were quite similar to the proportions during treatment. Nasal symptoms were most prevalent, however laryngeal, otologic, and ophthalmic symptoms of the patients' allergy were each indicated approximately 20% of the time. Further, as indicated in Figure 2, we found that the reduction in the number of symptoms was less during the first 6 months of therapy (29% reduction) and increased to a consistent level after 6 months (57%), which continued for more than 2 years (56%).

Overall, the average number of nasal symptoms reported per patient prior to IDT-based immunotherapy was 6.0. This decreased to 3.5 during active treatment, an overall decrease of 42%. Ophthalmic symptoms decreased from 2.7 to 1.6 (41%). Otologic symptoms decreased from 3.4 to 1.9 (44%). Laryngeal symptoms decreased from 3.0 to 1.4 (53%). This was a 45% decrease in all symptoms (nasal, ophthalmic, otologic, and laryngeal) reported after a patient was treated with immunotherapy.

DISCUSSION

Allergy and allergic rhinitis are extremely common conditions that have a considerable impact on the qual-

ity of life of the sufferer. Much advancement has occurred in the treatment of these ailments with improved nasal steroids, antihistamines, and IDT-based immunotherapy. Krouse and Krouse⁸ found that IDT-based immunotherapy was associated with a reduction in self-rated disability over time. Several other authors have recently developed validated questionnaires to assess outcomes of therapy of allergy-induced rhinosinusitis.

It is interesting to find, via thorough literature search, that limited publications have focused on outcomes of immunotherapy, specifically with end-organ target effects. Our data indicates there are multiple measurable end-organ targets that are affected by immunotherapy. Sneezing and postnasal drip were very common symptoms (87% and 83%, respectively, reporting these symptoms initially) that showed a decrease once immunotherapy had been initiated. Itching and swelling of the eyes, itching of the external auditory canal, and pressure and fullness feeling of the ear were also found to decrease in prevalence. Laryngeal issues including sore throat and the need to clear mucous from the throat in the morning were also reported by approximately one half of all patients in this study.

Further, we found that there was a significant decrease in the number of symptoms reported for each of our respected categories, which suggests association of the ear, nose, throat, and eye systems in allergy. This associated decrease once immunotherapy had been initiated also suggests and gives further support for the benefits of IDT-based immunotherapy in treating the appropriate allergy patient. It should be noted that although greater than 90% of patients felt improvement with immunotherapy, the only patients included in the current study were those who were undergoing immunotherapy. Patients who had either refused immunotherapy or did not tolerate it were not included in the analysis. We recognize this as a potential bias in the study. The design of this study did, however, allow us to examine a relatively large number of patients for an extended amount of time. It was interesting that we found a greater change in symptom reduction after 6 months of immunotherapy and that this reduction was maintained for more than 2 years.

Because of the difficulty of quantitative evaluation of the response to immunotherapy, several authors have developed allergy outcomes questionnaires, most of which focus on allergic rhinitis. Ideally, an allergy outcomes questionnaire would consist of a validated set of questions that addresses the multitude of symptoms associated with allergy in an otolaryngology practice as well as quality-of-life issues. A few of the recent outcome questionnaires found in the literature include the Sino-Nasal Outcome Test, the Rhinitis Outcomes Questionnaire, and the Rhinosinusitis Disability

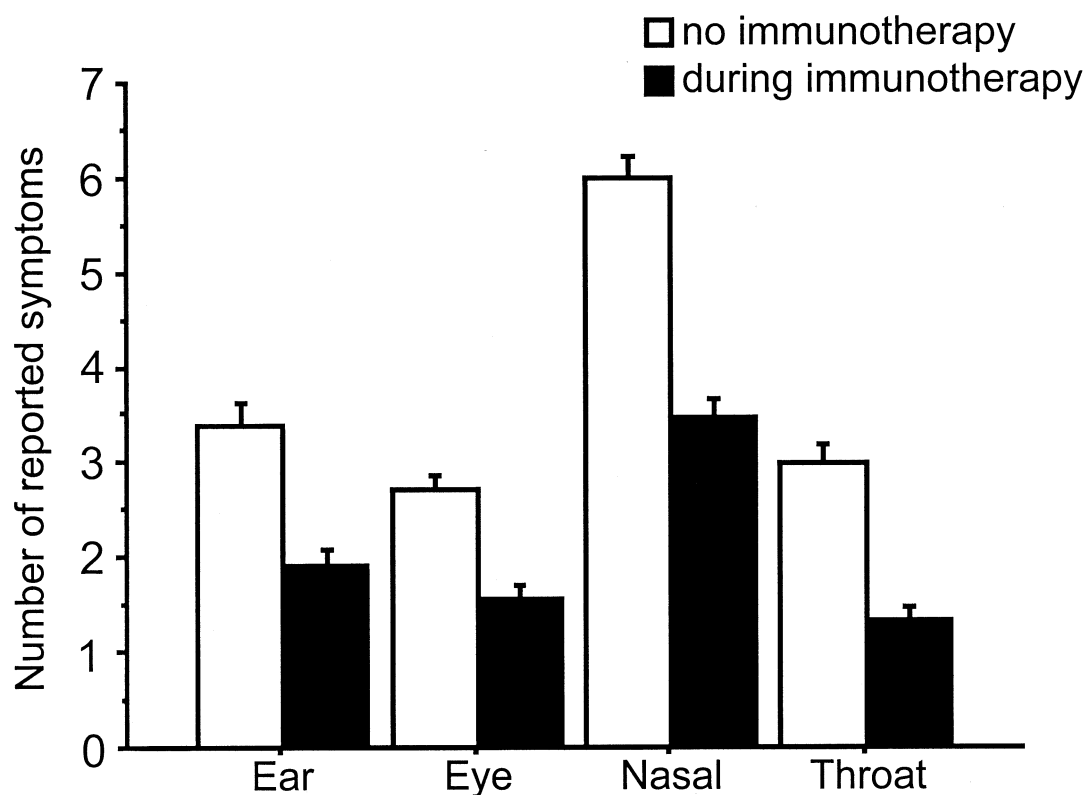


Fig 1. Symptoms reported before and during immunotherapy for each of the 4 categories. Statistically significant decreases in the number of symptoms were observed during therapy in each category.

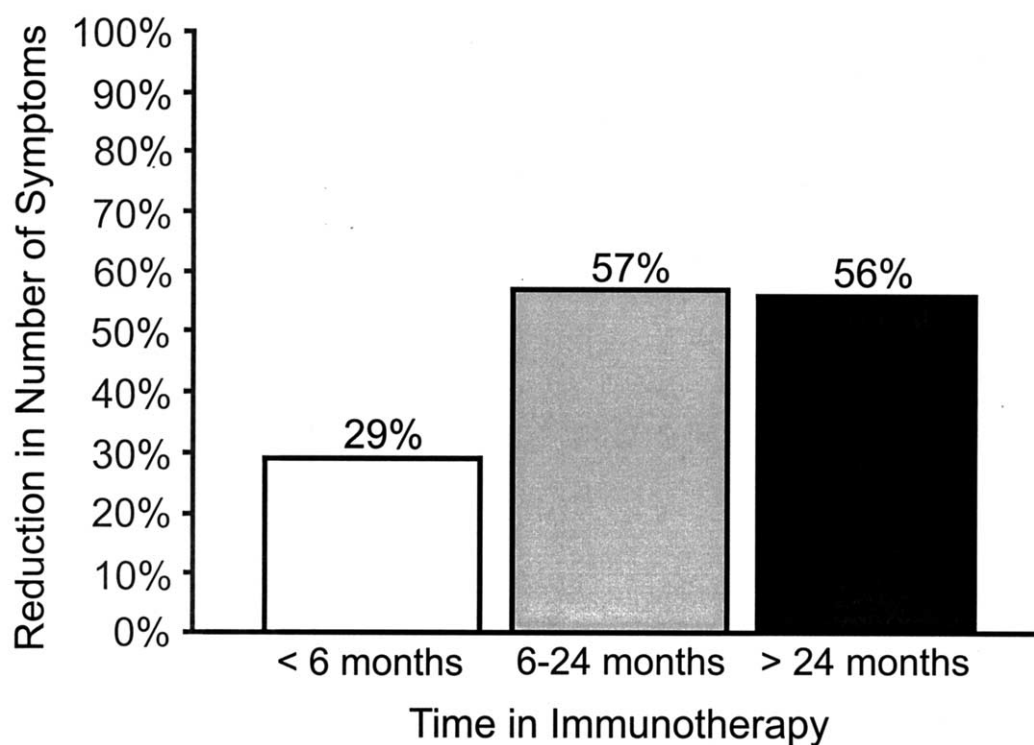


Fig 2. Percent reduction in the total number of allergy-induced symptoms over time during IDT-based immunotherapy. Patients reached maximum improvement by 6 to 24 months and that improvement was stable beyond 24 months.

Index. The Sino-Nasal Outcome Test (SNOT-20), is a disease-specific, health-related quality-of-life measure for rhinosinusitis, that includes both allergy-based symptoms (mainly nasal) and health-related quality-of-life issues. The Rhinitis Outcomes Questionnaire is a 5-part questionnaire developed to be administered in a private practice setting. It is focused mainly on allergic rhinitis treated with immunotherapy. This set of questions does address the association of ear, nose, throat, and eye symptoms, but provides limited data on quality-of-life issues. A third validated questionnaire, the Rhinosinusitis Disability Index, is a quality-of-life outcomes instrument that was created specifically for patients with rhinosinusitis and therefore does not include laryngeal or otologic symptoms. From our current study, we feel that the development of an outcome questionnaire that focuses not only on nasal symptoms but on the full range of head and neck allergy and quality-of-life issues will assist the practicing otolaryngologist in following the response to IDT-based immunotherapy.

Although nasal symptoms are probably the most common complaint of the allergy patient presenting to the otolaryngology clinic, we found that these patients also have a significant proportion of symptoms from the laryngeal, otologic, and ophthalmic systems. This study

indicates that there is a broad response to IDT-based immunotherapy in the head and neck, and this response appears to be consistent for a period of time over 2 years.

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REFERENCES

1. Nathan RA, Meltzer EO, Selner JC, et al. Prevalence of allergic rhinitis in the United States. *J Allergy Clin Immunol* 1997;99: S808-14.
2. Santilli J, Nathan R, Glassheim J, et al. Validation of the Rhinitis Outcomes Questionnaire (ROQ). *Ann Allergy Asthma Immunol* 2001;86:222-5.
3. Mabry RL. American Academy of Otolaryngic Allergy: skin endpoint titration. New York: Thieme; 1992.
4. Benninger MS, Senior BA. The development of the Rhinosinusitis Disability Index. *Arch Otolaryngol Head Neck Surg* 1997;123: 1175-9.
5. Piccirillo JF, Merritt MG, Richards ML. Psychometric and clinical validity of the 20 item Sino-Nasal Outcome Test (SNOT-20). *Otolaryngol Head Neck Surg* 2002;126:41-7.
6. Kemker BJ, Corey JP, Branca J, et al. Development of the Allergy Outcome Survey for allergic rhinitis. *Otolaryngol Head Neck Surg* 1999;121:603-5.
7. Derebery MJ, Berliner KI. Allergy and health-related quality of life. *Otolaryngol Head Neck Surg* 2000;123:393-9.
8. Krouse JH, Krouse HJ. Efficacy of immunotherapy based on skin end-point titration. *Otolaryngol Head Neck Surg* 2000;123:183-7.