Identification of Allergic Disease Among Users of Antihistamines

SHERYL L. SZEINBACH, PhD; P. BROCK WILLIAMS, PhD; PIETER MUNTENDAM, MD; and RICHARD D. O’CONNOR, MD

ABSTRACT

OBJECTIVE: Patients exhibit a multitude of symptoms that may or may not be allergic related. In this study, we examined the consistency between results obtained by a multiallergen-specific immunoglobulin E (IgE) test and frequent use (3 months or more) of prescribed antihistamines.

METHODS: A retrospective examination of 1-year prescription claims records from January 1, 2000, through December 31, 2000, for 4,643 patients enrolled in a 115,000-member managed care organization who received 1 or more prescriptions for an oral antihistamine (loratadine, fexofenadine, or cetirizine).

RESULTS: A total of 1,343 health plan enrollees who received an oral antihistamine prescription were continuously enrolled during the year 2000 and diagnosed with allergic rhinitis. Of these patients, 246 (18%) consented to a multiallergen-specific IgE test, and 159 patients (64.6%) had a negative IgE test result. A total of 163 patients were classified as frequent antihistamine users (3 or more antihistamine prescriptions), and 101 (62.0%) of these patients had negative test results. Our study demonstrated no relation between prescribed antihistamine use and patient sensitization status.

CONCLUSIONS: Only 35.4% of the patients who used an oral antihistamine and were diagnosed with an allergy tested positive to the multiallergen-specific IgE test, and only 38% of the patients with records of frequent antihistamine use and who were diagnosed as allergic tested positive to the multiallergen-specific IgE test. Apparently, there are patients taking medications prescribed for allergic rhinitis who are, in fact, not allergic, which is both wasteful economically and not allergy related. In this study, we examined the consistency between results obtained by a multiallergen-specific immunoglobulin E (IgE) test and frequent use (3 months or more) of prescribed antihistamines.

KEYWORDS: Allergic rhinitis, Multiallergen-specific IgE testing, Low-sedating antihistamines

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SYMBOLS

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Only recently has evidence surfaced to suggest that patient history and symptoms may not align well with the results obtained from diagnostic tests such as skin testing or multi-allergen-specific IgE testing. In one study, the accuracy of the diagnosis of a patient for a specific allergic condition by history alone compared with concordant skin testing and specific IgE measurements rarely exceeded 50% and, in some cases, was below 25%. Given this potential for discrepancy between history and true diagnosis, questions arise regarding the existence of similar discrepancies between prescribed antihistamine use and multiallergen-specific IgE testing.

In this study, we investigate whether the patterns of prescribed antihistamine use in a managed care facility were consistent with results obtained from a multiallergen-specific IgE test for allergy. Specifically, the UniCAP Phadiatop is a single laboratory test designed to determine the presence or absence (e.g., positive or negative) of specific IgE to a variety of common inhalant allergens (e.g., grass, ragweed, cat, and mite). In this study, the cut-off point for positivity for the specific IgE assays was 0.35 kUA/L, with test sensitivity and specificity reported at 100%. Test results were categorized as either positive or negative.

**Methods**

Prescription claim records for 4,643 patients enrolled in a 115,000-member health plan located in the southeast United States were examined retrospectively by 2 pharmacists to identify patients who received at least 1 prescription for a low-sedating antihistamine (LSA) in tablet or capsule form (cetirizine 5 mg or 10 mg, fexofenadine 60 mg, loratadine 10 mg, and all combinations with pseudoephedrine). Of these 4,643 patients, there were 1,343 patients with a diagnosis of allergic rhinitis (ICD-9-CM 477.0, 477.8, and 477.9 for pollen, other allergens, and unspecified, respectively). Antihistamine use was defined as follows:

- **Positive IgE Test Result**
  - Frequent Use: No (28.7%)
  - Frequent Use: Yes (71.3%)

- **Negative IgE Test Result**
  - Frequent Use: No (36.5%)
  - Frequent Use: Yes (63.5%)
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**Table 1** Cross Tabulation of Laboratory Multiallergen Specific IgE Test Results (±) and Frequent Antihistamine Use (Yes/No)

<table>
<thead>
<tr>
<th>Screening Result:†</th>
<th>Frequent Use*</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>Negative test</td>
<td>58</td>
<td>101</td>
<td>159</td>
<td></td>
</tr>
<tr>
<td>% within nonallergic</td>
<td>36.5</td>
<td>63.5</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>% within frequent use</td>
<td>69.9</td>
<td>62.0</td>
<td>64.6</td>
<td></td>
</tr>
<tr>
<td>% of total</td>
<td>23.6</td>
<td>41.1</td>
<td>64.6</td>
<td></td>
</tr>
<tr>
<td>Positive test</td>
<td>25</td>
<td>62</td>
<td>87</td>
<td></td>
</tr>
<tr>
<td>% within allergic</td>
<td>28.7</td>
<td>71.3</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>% within frequent use</td>
<td>30.1</td>
<td>38.0</td>
<td>35.4</td>
<td></td>
</tr>
<tr>
<td>% of total</td>
<td>10.2</td>
<td>25.2</td>
<td>35.4</td>
<td></td>
</tr>
<tr>
<td>Nonallergic and allergic</td>
<td>83</td>
<td>163</td>
<td>246</td>
<td></td>
</tr>
<tr>
<td>% of total</td>
<td>33.7</td>
<td>66.3</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

*Frequent antihistamine use defined as 3 or more prescriptions for low-sedating antihistamines during the continuous 12-month enrollment period.
†Screening test results available only for those who were lab tested. All tests conducted with the multiallergen-specific IgE test.

Chi-square test ($\chi^2 = 1.5; P<0.225$) for the convenience sample (N = 246); IgE is immunoglobulin E.

Discussion

The initial clinical diagnosis of an allergic condition was supported for 35.4% of the patients who had the multiallergen-specific IgE test. Although the treatment of rhinitis with antihistamines is often used to provide diagnostic evidence of an allergic etiology, it has been estimated that as many as 50% of patients with rhinitis may not have allergic rhinitis.19,20 Thus, in some situations, short-term or intermittent use of these medications is warranted to treat conditions such as nasal congestion, rhinorrhea, sneezing, itching, and hyposmia. However, frequent use (3 months or more) of prescribed antihistamines would suggest the need for more specific evaluation or additional follow-up.

The lack of a significant difference in frequent antihistamine use and the presence or absence of inhalant allergy in this patient population suggests that routine history and physical examination may not always provide accurate evidence to discern allergic from nonallergic rhinitis.5 Considering that the results of this study are consistent with findings from previous reports of confirmed allergy (43%, n= 975),21,22 our findings suggest the need for more extensive patient evaluation criteria. Although patients provide a comprehensive overview of their current health status, additional opportunities exist for clinicians in patient screening and evaluation. For example, patients who present with multiple allergic-like symptoms would undergo preliminary evaluation by trained clinicians and practitioners. Decision protocols can be developed and standardized to ascertain whether perceptual differences in judgment have possibly influenced conclusions drawn from the patient history and evaluation.13 After examining patient history and evidence of allergic etiology, or patients appear unresponsive to medications, objective tests such as the multiallergen-specific IgE test may be performed.

At the time of this study, loratadine was available only by prescription, but the availability of loratadine over the counter (OTC) at year-end 2002 begs examination of the means to attain the optimum cost benefit from verification of true allergy in frequent users of antihistamines. While OTC loratadine costs less than $20 per month of therapy, most drug plans in managed care organizations (MCOs) cover prescription oral antihistamines that have average wholesale prices that range from $75 to $105 for a 30-day supply.23 The average price paid per spe-
cific IgE determination ranges from $10 to $12 per allergen ($7.23 for Medicare). The Medicare median patient charge for allergy testing, which includes 12 to 16 profile allergens and total IgE ($20) was approximately $150 to 175 per profile and ranged from $50 to $500, depending on the type of test (e.g., skin, blood) and the number of allergens evaluated.²⁴ Although these costs, to some extent, may be covered by a third-party plan, patients, providers, and MCOs should evaluate short-term and long-term benefits of serum allergy testing.

From a managed care perspective, optimal strategies for therapy would begin by accurately identifying patients who would benefit from specific IgE testing. Results from this study suggest that confirmation of allergic disease may be more complex, perhaps involving the cooperation of both family physicians and allergists. Primary care physicians might perform initial evaluation, testing, and treatment involving the short-term use of antihistamines and, with patients, evaluate patient responsiveness to drug therapy. Persistent or more-severe symptoms may require further evaluation and referral. Allergy testing may be more beneficial when patients are stratified by severity and persistence of allergy symptoms, magnitude of direct costs (e.g., physician visits, oral antihistamines), and indirect costs (e.g., diminished productivity). These suggestions present opportunities for managed care physicians and pharmacists to work together efficiently to create an environment to improve patient management through initiatives that focus on diagnostic accuracy. Hence, consideration should be given to the additional benefits of testing and the contribution that appropriate prescribing would make toward improving patient outcomes and possibly reducing health care and social costs.

Limitations

The extent to which patients are affected by allergic rhinitis may be a function of seasonal fluctuations characteristic of the geographic region (southeastern United States) of this MCO. Additionally, survey completion was not designed to necessarily coincide with the annual period during which symptoms were experienced. Hence, the absence of particular symptoms at that time did not preclude the presence of seasonal allergic rhinitis. However, seasonal affects may be of no consequence since the IgE test is unaffected by antihistamine use. Moreover, the presence of IgE is not affected by the season in which the test is performed.

Conclusions

By far, the most common—but not only—reason for prescribing LSAs is for symptoms with a suspected allergic etiology. Our data suggest that either LSAs are prescribed indiscriminately or that the sequencing of testing and treatment needs further notification. Notwithstanding consideration of medication side effects, economic considerations, and the potential for escalating costs associated with the advent of more expensive allergy treatment options (e.g., leukotriene receptor antagonists, anti-IgE), ensuring the existence of allergic etiology may be more beneficial to patients (e.g., reduced office visits, improved quality of life) and increasingly important to managed care providers. Practitioners and clinicians might use objective means such as multiallergen-specific IgE testing in conjunction with other evidence such as patient symptoms and history to confirm the allergic basis of disease.

DISCLOSURES

Funding for this study was provided by an unrestricted grant from Pharmacia Corporation and was obtained by author Pieter Muntendam. Results from this study were presented at the American College of Osteopathic Family Physicians (ACOFP) Meeting, Philadelphia, Pennsylvania, March 28, 2001, and at the Aspen Allergy Conference, Aspen, Colorado, July 26, 2001. Author Sheryl L. Szeinbach served as principal author of the study. Study concept and design were contributed primarily by Szeinbach and Muntendam. Analysis and interpretation of data were contributed by Szeinbach and authors P. Brock Williams and Richard D. O’Connor. Drafting of the manuscript was primarily the work of Szeinbach and Williams, and its critical revision was the work of all authors. Statistical expertise was contributed by Szeinbach and Williams, and administrative, technical, and/or material support was provided by Szeinbach and Muntendam.

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