Brief Report

Link Between Patient Preferences and Treatment Outcomes in Seasonal Allergic Rhinitis: An Empiric Investigation

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ABSTRACT

In a multicenter, parallel-group, double-masked, randomized study, two questionnaires were administered to a clinical study population to identify which specific symptoms of seasonal allergic rhinitis patients perceived as most important to relieve (personal preferences) and to learn whether any relationship existed between patient preferences and the severity of their symptoms during treatment with antihistamines. The group was composed of 256 males and 313 females. Their mean age was 32.4 years, and mean duration of seasonal allergic rhinitis was 14.5 years, with mean age of onset of 17.7 years. After receiving placebo for 1 week, patients were randomly allocated to receive an antihistamine (fexofenadine or loratadine) for 2 weeks. Patient preferences for relief of individual allergy symptoms (rhinitis; sneezing; itchy, watery, red eyes; itchy nose, palate, or throat) and related conditions (fatigue, physical limitations) were scored using 2 different questionnaires before treatment (0-to-10 category rating scale for assessing the 4 symptoms of allergic rhinitis) and after receiving placebo for 1 week (Feeling Thermometer). Symptom severity was reported in patient diaries after 1 and 2 weeks of antihistamine treatment and was measured by patient self-assessment. All symptoms were considered by the patients to be important to relieve, the most important being itchy, watery, red eyes and rhinorrhea. The severity of allergy symptoms was consistently related to the importance of symptoms identified before treatment. Therefore, including patient preferences in medical evaluations might be a useful tool in evaluating the success of their treatment. ***Key words:*** seasonal allergic rhinitis, patient preferences, fexofenadine, loratadine.

INTRODUCTION

Health care quality has traditionally been defined by health care providers, with patients cast as passive recipients. It would be logical to assume that involving pa-

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tients in decision making about their care would improve their perception of health care quality. Compliance with treatment regimens may be compromised if the treatment goals of the health care worker and the patient do not coincide.[1] A basic assumption of outcomes research that measures only quantifiable variables such as physical or physiologic factors (eg, white blood cell count, blood pressure, or serum cholesterol levels) is that such measures are important to patients. However, patients are primarily concerned with improving their daily functioning rather than with medically defined physiologic functions whose effects they may not be able to discern.[2]

Preference refers to the level of desirability that a person associates with a particular health state, treatment process, duration of treatment or illness, or level of participation. Preference-based scores are a useful complement to symptom indices or quality-of-life scores. Health care providers and patients may hold different views about which attributes of a health state are important. The changing dynamics of modern health care, combined with ethical considerations, have led to an attempt to understand the foundations of patient decision making.[3]

Allergies and allergic symptoms may have a substantial impact on an individual's quality of life. The symptoms can affect daily activities, including work productivity, learning performance, and interpersonal relationships.[4] Symptoms associated with common allergies generally are not life threatening. In clinical decision making, health care professionals must consider to what extent symptoms affect each patient. Physicians and patients need information regarding the impact of treatment on the patient's quality of life and performance in the workplace, at school, and at home. Patients tend to evaluate a medication based not only on its clinical effectiveness, but also on how it affects all aspects of their lives.[2]

Antihistamines are the most commonly used antiallergy medications.[5] They act as competitive antagonists of histamine at the H_1-receptor site responsible for stimulating sensory nerves and increasing vascular permeability and mucus production. Therefore, antihistamine activity diminishes pruritus, sneezing, and rhinorrhea.[6]

Patients' commitment to their personal health care greatly contributes to compliance.[7] A focus on improving symptoms identified as most bothersome by each patient more accurately reflects whether the patient perceives treatment as successful.

In this study our objectives were the following: to identify which specific symptoms were perceived by patients to be the most important to alleviate (personal preferences); to investigate the relationship between patient preferences for relief of symptoms and the severity of symptoms following 2 weeks of treatment with antihistamines; and to investigate the influence of compliance history with allergy medication and patient personal preferences on alleviation of specific allergy symptoms.

The efficacy and safety results of the present study are not the subject of this paper and are reported elsewhere (unpublished data, Hoechst Marion Roussel, Canada).

PATIENTS AND METHODS

Patients

All patients were ≥12 years of age and had had seasonal allergic rhinitis during spring of the 2 previous years. Seasonal

allergic rhinitis was defined as immunoglobulin E–modulated immunologic response to allergens released during tree, grass, or weed pollination, that is characterized by sneezing, rhinorrhea, nasal congestion, and nasal pruritus.[8] Participants had had a positive epicutaneous response to antihistamine; a total reflective score of >6 for the previous 12 hours; and 2 or more symptoms of seasonal allergic rhinitis rated as moderate or severe, with no symptom rated as very severe.

Pregnant or lactating women, patients who had contracted upper respiratory tract infections within 30 days preceding the start of the study, and patients with significant diseases (ie, malnutrition, blood dyscrasia, renal or hepatic insufficiency, chronic infection, malignancy malabsorption, or any other clinically significant cardiovascular, hepatic, neurologic, endocrine, or other major systemic disease that would make implementation of the protocol or interpretation of the results difficult), or a history of alcohol or drug abuse or hypersensitivity to the study medications were excluded.

Study Design

A multicenter, parallel-group, double-masked, randomized design was used for this questionnaire-derived assessment. At study entry (visit 1), the total symptoms score (TSS) questionnaire was administered to all patients to assess their preferences for relief of specific allergy symptoms. At the same time, a symptom-severity measure was also administered. At visit 1, participants also completed a questionnaire describing the history of their allergy medication use, listing which specific medications they usually took for symptom relief and how often. The following symptoms were assessed: sneezing; rhinorrhea; itchy nose, palate, or throat; and itchy, watery, red eyes. After receiving placebo for 1 week (visit 2), a second questionnaire on patient preferences, distinct from the first one, was administered. The patients were then randomly allocated to receive 2 weeks of either fexofenadine 60 mg twice a day or loratadine 10 mg once a day (Figure 1).

The protocol and the informed consent document were approved by each investigator's ethics review committee or independent review committee. The study was conducted at 20 Canadian clinical sites. Each patient was required to sign a written informed consent form that explained the purpose of the study, the risks and benefits of participation, and provided assurance of confidentiality.

Outcome Measures

Efficacy, which was not the objective of the present study, was determined on a daily basis using the TSS—a sum of the individual scores on the patient-reported symptom severity scale (0 to 4 points, with 4 being the most severe) for each of 4 symptoms: sneezing; rhinorrhea; itchy nose, palate, or throat; and itchy, watery, red eyes.

Personal Preference

Personal preference was defined as the importance to each patient of relieving each allergy symptom (ie, most important to relieve or not most important to relieve). A MEDLINE® search failed to identify an existing, appropriate, well-validated instrument to address our objectives; we therefore developed instruments specifically for our study.

A visual analog scale was selected for its simplicity in measuring subjective phenomena. The scale has been studied extensively and has been shown to be reli-

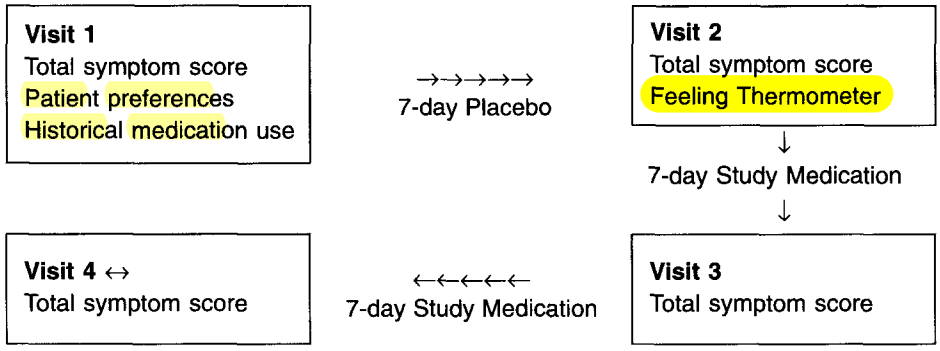

Figure 1. Study design and timing of questionnaire administration.

able and valid in most circumstances.[9] The advantages and disadvantages of using this type of scale have been reported elsewhere.[10] The "Assessment of Patient Preferences for Relief of Symptoms" and the "Feeling Thermometer" instruments were developed to assess precisely the importance of relieving each allergy symptom as presented in the patients' daily diary. In the patient-preference assessment, patients are asked to rate the importance of relieving each allergy symptom and related condition on a scale (0 = relief is not important at all; 10 = relief is very important). The Feeling Thermometer indicates the degree to which patients are bothered by allergy symptoms (0 = least bothersome; 10 = most bothersome).

Efficacy was determined daily using the patient-rated TSS. Both the efficacy (symptom severity) and the preference measurements evaluated the same 4 symptoms: sneezing; rhinorrhea; itchy nose, palate, or throat; and itchy, watery, red eyes. Two allergy-related conditions (fatigue and physical limitations) were also assessed. Therefore, the face and content validity, indicating that the instruments were assessing the desired qualities, were met in our opinion.

Instruments were not administered a second time to determine reliability. Basing the reliability of the instruments on a single administration and the calculation of the Cronbach's alpha was not an optimal approach because we did not assume from the start that each score would correlate with other scores. On the contrary, we expected preference scores to be quite different from one another. The results, however, were contrary to our expectations.

At recruitment, the questionnaire was used to assess patient preferences: patients were requested to indicate the importance of relieving 4 allergy symptoms, forming the basis of the TSS, and 2 allergy-related conditions, using a 0-to-10 category rating scale. After receiving placebo for 1 week (visit 2), the preference scores for symptom relief were also assessed using the Feeling Thermometer.

These scores were compared with scores obtained using the previous category rating scale. Because the Feeling Thermometer questionnaire was admin-

istered after receiving placebo for 1 week, it was assumed that the derived preference scaling factors might reflect the true attributed value without reference to a specific medication. For each symptom and condition, the mean and median of the category rating scores from the rating scale were calculated. To define the influence of previous medication on preference baseline assessment, the mean scores were also estimated for patients on the basis of medication used in the past year. Moreover, patient preferences were estimated by compliance group and by sex. Patients' customary dosages and frequency were also included. The correlation among symptoms was then assessed.

Personal Preferences and Allergy Symptom Scores

Following treatment with 1 of the active medications (fexofenadine 60 mg twice a day or loratadine 10 mg once a day), patients were classified according to the specific symptom they identified as most important to relieve in the baseline category rating (most important or not most important), regardless of treatment group.

Symptom severity scores were available from patient diary entries during treatment. Patients indicated the severity of each symptom on a scale of 0 to 4 points, with 4 being the most severe. For each symptom, mean symptom scores were calculated and correlated to the level of importance (most important or not most important to relieve) indicated at baseline.

Statistical Analysis

The distribution of the symptoms rated as the most important to be relieved in the 2 study treatment groups was checked in contingency tables to assure comparability of groups. Correlation coefficients (Spearman's rank-order coefficient, rho) among symptoms for category rating scores were estimated to assess the relationship between the patients' personal preferences and the severity of symptoms. Because TSS is the calculation of a mean from ordinal values, parametric statistical analyses were deemed appropriate, particularly since the distribution of this variable was normal. Parametric tests are considered to be acceptable for evaluating visual analog scales.[9]

RESULTS

The study population consisted of 256 males and 313 females with a mean age of 32.4 years and a mean body mass index of 25.4; mean duration of seasonal allergic rhinitis was 14.5 years, with a mean age at onset of 17.7 years.

Upon recruitment, patients completed the category rating scale questionnaire, indicating which symptoms they would like to relieve. Following the 7-day placebo period, 491 patients completed the Feeling Thermometer questionnaire dealing with their preferences. The 73 patients who did not complete the Feeling Thermometer questionnaire were excluded from the clinical study and, therefore, could not be assessed using this measurement.

Symptom Preference

All allergy symptoms were rated as important to relieve (mean ≥6.1), indicating that patients seem to be seeking relief of all symptoms. On a 0-to-10 rating scale, the participants attributed a value of >6 (interquartile range containing 50% of observations), primarily between 7 and 9, to each symptom. Mean category scores in-

Table I. Preference scores.

	Before Treatment		After 1 Week of Placebo	
	Mean (SD)	Median (Interquartile Range)	Mean (SD)	Median (Interquartile Range)
Allergy symptoms				
Itchy nose, palate, or throat	7.6 (2.5)	8 (6–10)	6.5 (2.5)	7 (5–8.5)
Itchy, watery, red eyes	8.0 (2.5)	9 (7–10)	7.1 (2.6)	8 (5–9.3)
Rhinorrhea	8.0 (2.5)	9 (7–10)	7.3 (2.4)	8 (6–9.5)
Sneezing	7.2 (2.6)	8 (5–9.8)	6.1 (2.8)	7 (4–8.5)
Allergy-related conditions				
Fatigue	7.0 (3.0)	8 (5–9.8)	NA	NA
Physical limitations	6.5 (3.3)	7 (4–9.5)	NA	NA

NA = not applicable.

dicated that itchy, watery, red eyes and rhinorrhea were given the greatest importance. Fatigue and physical limitations were relatively less important (mean scores 7.0 and 6.5, respectively).

Preference measurements completed at the end of the placebo period using the Feeling Thermometer indicated that, overall, the mean scores were slightly lower than those obtained using the 0-to-10 category rating scale prior to the study; however, results were similar in that patients indicated that rhinorrhea and itchy, watery, red eyes were the most important symptoms to relieve. The results obtained prior to treatment and after receiving placebo for 1 week are summarized in Table I. No statistically significant differences were observed between the 2 observations for any of the parameters evaluated.

The association between symptoms indicated that all correlation coefficients were significant at the $P < 0.01$ level; however, the correlations were weak. The 2 highest correlations were those between sneezing and rhinorrhea (0.52), and between fatigue and physical limitations (0.55) (Table II).

Overall, women assigned higher scores to relief of allergy symptoms than men ($P < 0.001$ for itchy nose, palate, or throat; $P < 0.05$ for fatigue). Patients who were compliant with previous treatments assigned lower severity scores ($P < 0.05$ for rhinorrhea and physical limitations). No significant differences were observed between the 2 treatment groups.

Although patients in the 2 treatment groups received their respective medications (fexofenadine or loratadine) under identical clinical trial conditions, scoring of allergy symptoms during the treatment period was consistently linked to the importance of symptoms identified prior to treatment. Differences in efficacy scores between most important (1) and not most important (2 to 4) were statistically significant for itchy nose, palate, or throat; itchy, watery, red eyes; and rhinorrhea ($P < 0.01$) (Table III).

The distribution of patients by personal preference was equivalent in the 2 treatment groups.

When patients were stratified according to the medications they had been taking prior to the study (none, Claritin® [Scher-

Table II. Correlation* between symptoms: Category ratings.

	Itchy, Watery, Red Eyes	Itchy Nose, Palate, or Throat	Rhinorrhea	Sneezing	Fatigue
Itchy nose, palate, or throat	0.37	—			
Rhinorrhea	0.30	0.34	—		
Sneezing	0.33	0.29	0.52	—	
Fatigue	0.41	0.36	0.28	0.23	—
Physical limitations	0.40	0.29	0.24	0.27	0.55

*All coefficients are statistically significant at the 0.01 level.

ing, Pointe-Claire, Quebec, Canada], Claritin® Extra [Schering, Pointe-Claire, Quebec, Canada], Reactine® [Pfizer, Kirkland, Quebec, Canada], Seldane once-a-day®, [Marion Merrell Dow, Laval, Quebec, Canada]), rhinorrhea and itchy, watery, red eyes were again the symptoms that patients felt were the most important to alleviate. Patients who had not taken any medications for their allergies prior to the study showed the lowest preference scores, perhaps indicating that their initial symptoms were less severe than those experienced by patients who had taken medications previously.

Baseline assessment indicated that women ascribed higher importance to relieving allergy symptoms than men.

DISCUSSION AND CONCLUSIONS

Symptom severity while receiving treatment was consistently linked to the importance of symptoms identified prior to treatment, although patients received their respective medications (fexofenadine or loratadine) under the same study conditions. Because patient preferences were equally distributed in the 2 treatment groups, this variable did not introduce any bias for the efficacy results.

The mean preference scores on the Feeling Thermometer (after receiving placebo for 1 week) were slightly lower than those obtained at baseline on a 0-to-10 category rating scale, although the patterns of response were similar. However, because the values were obtained from 2 different instruments administered at 2 different time periods, they were not directly comparable.

Any previous medication, whether used correctly or incorrectly (underused or overused), could have introduced a bias when preference baseline values were measured.[5]

Compliant patients assigned lower preference scores than noncompliant patients. The degree of patient compliance was determined by comparing the pattern of medication utilization, as reported in a product utilization questionnaire, to the recommended regimens.[5] Many factors could explain this relationship. It is assumed that because compliant patients take allergy medications at the appropriate dosage, they are less likely to experience allergies.[5] Thus they would be expected to rate their symptoms as having less importance. Conversely, because noncompliant patients are less likely to receive correct doses, their allergy symptoms tend

Table III. Mean symptom severity score per treatment period for patients grouped according to symptom preferences.

	Itchy Nose, Palate, or Throat*		Itchy, Watery, Red Eyes*		Rhinorrhea*		Sneezing	
Symptom preference rank	1	2–4	1	2–4	1	2–4	1	2–4
Mean severity score after 1 week of treatment	1.55	1.25	1.53	1.19	1.66	1.44	1.17	1.03
Mean severity score after 2 weeks of treatment	1.43	1.17	1.39	1.11	1.65	1.35	1.13	0.99

Symptom preference rank: 1 = most important to relieve; 2–4 = not most important to relieve.
*$P < 0.01$ most important versus not most important.

not to be relieved. Therefore, they may attribute a higher importance to their symptoms. It would then be expected that if a patient's allergies are not relieved, the patient would be dissatisfied and would tend to be less compliant.[11]

One of the limitations of the study was that the reliability measure of the instruments was not assessed by administering the questionnaires a second time to the same population. Basing the reliability of the instruments on a single administration and the calculation of Cronbach's alpha was not an optimal approach because it was not assumed from the start that each score would correlate with other scores. On the contrary, we expected the preference scores to be quite different from one another, but this was not the case. No other reliability test was conducted.

Knowing which symptom a patient wants to relieve the most can help to predict the level of satisfaction with a treatment.[1,7,12] Clinicians committed to improving patient outcomes must recognize outcomes that are valued by patients and that shape their motivation to comply. Understanding the patient's perspective requires that the patient be an active participant in the research.[2] Patients' self-rating of treatment effects should always be included when evaluating a treatment. Techniques for surveying patients about their preferences for health outcomes have been applied primarily in research settings, having only recently been introduced in clinical practice.[1]

Patients who are integral partners in making medical decisions are more satisfied with their care, more adherent to recommendations, and experience better health outcomes.[7] It has been demonstrated that patient satisfaction can influence the efficacy of interventions, as well as adherence behavior such as compliance and care-seeking,[2,13–15] and should be included as a measure of the quality of health care.[16] Shared decision making may lead to increased satisfaction with the decision and consequently to better compliance and better health outcomes.[17] Based on the observations from this questionnaire-derived survey, the sequence of events shown in Figure 2 is proposed.

Few validated instruments for the measurement of satisfaction are currently available. Continued research should better define the measurement of satisfaction

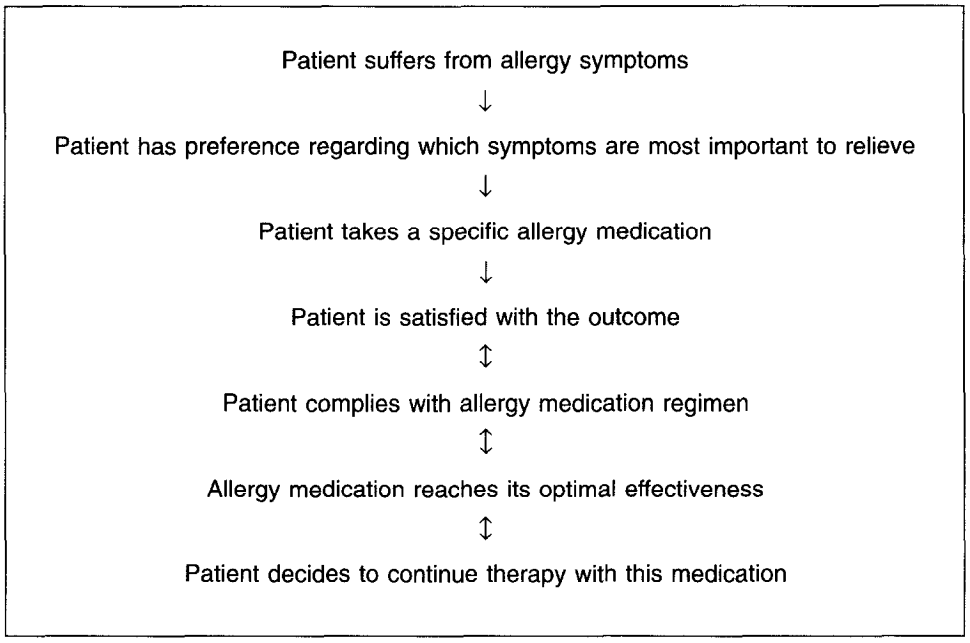

Figure 2. Proposed mechanism of the effect of patient preference on the success of allergy drug therapy selected, based on patient preference.

and clarify its theoretical and substantive meaning. A framework is needed to determine what information will most facilitate patients' taking an integral role in their health care decisions.[7] Other work to clarify the correlation between satisfaction and other variables is also needed. The practice of developing ad hoc instruments should be replaced by the use of well-validated instruments that combine cross-setting and setting-specific items.[14]

Until recently, consumers' views have not been regarded as a relevant contribution to the evaluation of medical care. In a MEDLINE® search of the literature, this was the only study to evaluate the significance of patient preference in seasonal allergic rhinitis used as an indirect measure of patients' satisfaction with their treatment. The results of this study reinforce the importance of patient participation in medical decision making to the success of their treatment. In future research, including patient preferences in medical assessments could be expanded to other variables, such as patient preferences toward medication costs, formulations, and side effects.

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