Original Article

Determinants of Incomplete Asthma Control in Patients with Allergic Rhinitis and Asthma

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What is already known about this topic? Allergic rhinitis has a major impact on the asthma condition.

What does this article add to our knowledge? The activity of allergic rhinitis had a significant influence on the degree of asthma control after adjusting for many relevant clinical factors.

How does this study impact current management guidelines? Evaluation of the activity of allergic rhinitis in patients with asthma and adequate treatment are likely to improve asthma control.

BACKGROUND: Characterizing associations between the upper and lower airways is important for asthma management.
OBJECTIVES: This study aimed to assess the determinants of incomplete asthma control in patients with allergic rhinitis (AR) and asthma.
METHODS: Multiple factors including age, sex, atopy, smoking history, medication use, Asthma Control Questionnaire (ACQ) score, FEV_1, fraction of exhaled nitric oxide (FENO), and rhinitis questionnaire score were examined. AR was defined by rhinitis symptoms and the sensitization to inhaled allergens. ACQ was used to dichotomize the subjects into the incompletely controlled group (ACQ score ≥0.75) and the well-controlled group. The factors that contribute to incomplete asthma control were assessed by a multivariate analysis.
RESULTS: A total of 260 patients with AR and asthma were enrolled and 108 patients (42%) were classified as incomplete asthma control. The incompletely controlled group was older ($P < .05$), and had more airflow limitation, more airway inflammation, and more severe rhinitis symptoms (all $P < .001$). In contrast, the well-controlled group was more likely to be taking nasal corticosteroids (NCSs) ($P < .01$). In a multivariate model adjusted by age, asthma treatment, airflow limitation, and FENO, persistence and severity of rhinitis (odds ratio [OR], 2.57; 95% CI, 1.41-4.70, and OR, 2.00; 95% CI, 1.10-3.65) and nonuse of NCSs (OR, 3.83; 95% CI, 1.50-9.81) were independently associated with incomplete asthma control.
CONCLUSIONS: The persistence and severity of AR and the use of NCSs were associated with the level of asthma control in patients with AR and asthma. Further studies are required to determine whether appropriate treatment of rhinitis would improve asthma control. **(J Allergy Clin Immunol Pract 2016;■:■-■)**

Key words: *Airflow limitation; Airway inflammation; Atopy; Exhaled nitric oxide; Inhaled corticosteroids; Nasal corticosteroids*

Allergic rhinitis (AR) has a major impact on asthma condition.[1-4] Although the associations between the upper and lower airways are not entirely understood, pathophysiologic events critical to the clinical manifestations of AR and asthma are similar.[5-7] Multiple factors have been associated with loss of asthma control in patients with AR and asthma, including rhinitis symptoms, blood eosinophil counts, and sinonasal mucosa thickness assessed by coronal computed tomography.[7-10] However, most of these studies defined AR by clinical symptoms and/or patient questionnaire, and many studies were *post hoc* analyses.[9,10] Moreover, despite its high prevalence, there are few studies on the effect of AR therapy on asthma control.[7] To date, the factors that are associated with asthma control have not been fully elucidated in patients with confirmed atopic AR and asthma.

In this cross-sectional study, we initially evaluated the level of asthma control in adult patients with AR and asthma on inhaled corticosteroid maintenance therapy. AR was defined by rhinitis symptoms and the sensitization to inhaled allergens on the basis of Allergic Rhinitis and its Impact on Asthma (ARIA)[1] guidelines. Next, the individual factors that contribute to impaired asthma control were assessed by a multivariate logistic regression model.

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Abbreviations used
ACQ- Asthma Control Questionnaire
AR- Allergic rhinitis
ARIA- Allergic Rhinitis and its Impact on Asthma
FENO- Fraction of exhaled nitric oxide
NCS- Nasal corticosteroid
OR- Odds ratio

METHODS

Study design and patients

This was a cross-sectional study. The patients enrolled came from our hospital-based respiratory clinic. A population of 410 nonsmoking patients with asthma was recruited during the pollen season in Japan (from February 2013 to April 2013). We chose this period to examine whether the activity of AR would affect asthma control in patients. All patients had a history of episodic dyspnea, wheezing, and documented airway reversibility and/or airway hyperresponsiveness. According to Global Initiative for Asthma guidelines,[11] asthma therapy was standardized and included inhaled corticosteroid with or without long-acting β2-agonist, leukotriene antagonist, or theophylline. Current smokers and patients with more than 10 pack-year smoking history were not included. Also, patients with poor adherence to asthma therapy (defined as <80% adherence calculated by dividing the number of days supplied for a medication by the number of days between the visits) or with other pulmonary diseases such as chronic obstructive pulmonary disease were excluded. We examined atopy, Asthma Control Questionnaire (ACQ) score, forced vital capacity, FEV_1, fraction of exhaled nitric oxide (FENO), and rhinitis questionnaire score approved by the Japanese Global Initiative for Asthma and ARIA committee.[1,2] Serum specific IgE level for common inhaled allergens (house dust mite, cedar, ragweed, cocksfoot, dog allergen, and cat allergen) was measured by using the ImmunoCAP system (Pharmacia Diagnostics, Uppsala, Sweden). To detect atopy more reliably, positive specific IgE levels were defined as more than 0.7 UA/mL. Positive specific IgE to at least 1 allergen was assumed to confirm atopy. In the present study, patients older than 20 years with confirmed atopic AR and asthma were selected and the subsequent analyses were performed. This study was approved by the local ethics committee (institutional review board 526). Informed consent for using the data was obtained from all patients.

Study assessments

The rhinitis questionnaire validated by Ohta et al[2] was used to assess the nasal symptoms (Table I).[1] AR was suggested if there was a positive answer to the following question: Do you have any of symptoms including watery runny nose, sneezing, nasal obstruction, or itchy nose when you do not have a cold? The ARIA classification, persistence and severity of AR, and its impact on quality of life were also evaluated.[1] The ACQ is a composite measure that assesses the asthma condition according to 5 items.[12,13] The overall score was the mean of the 5 responses, and an ACQ score of 0.75 or more was considered to indicate incompletely controlled asthma.[12] Both questionnaires have been used in earlier studies.[2,8] The forced vital capacity and FEV_1 were measured using a dry rolling seal spirometer (CHESTAC-8800; Chest, Tokyo, Japan). The FENO was measured by an online nitric oxide analyzer at a constant flow rate of 50 mL/s (NIOX MINO; Aerocrine, Solana, Sweden). Repeated exhalations were performed to obtain 2 acceptable measurements that agreed within 10% deviation, and the average of these 2 values was registered.[14]

TABLE I. AR patient questionnaire[1]

Question 1, Do you have any of these symptoms?*		
Watery runny nose	Yes	No
Sneezing, especially violent and in bouts	Yes	No
Nasal obstruction (feeling of being unable to breathe through your nose)	Yes	No
Itchy nose	Yes	No
Watery, red, itchy eyes	Yes	No
Question 2, What are these symptoms like?†		
Do you have symptoms more than 4 d/wk?	Yes	No
Do you have symptoms for more than 4 wk in a row?	Yes	No
Do your symptoms disturb your sleep?	Yes	No
Do your symptoms restrict your daily activities (sports, leisure, etc)?	Yes	No
Do your symptoms restrict your participation in school or work?	Yes	No
Do your symptoms seem troublesome to you?	Yes	No

Persistent rhinitis means that the symptoms are present for more than 4 d/wk and for more than 4 wks in a row. Moderate/severe rhinitis means that 1 or more of the following items are present: sleep disturbance, impairment of daily activities, leisure, and/or sport, impairment of school or work, troublesome symptoms.
*Question 1 asks about symptoms highly specific to AR.
†Question 2 asks the persistence and severity of rhinitis and impact on quality of life.

STATISTICAL ANALYSIS

The study subjects were dichotomized into 2 groups on the basis of ACQ scores. We labeled those with scores of less than 0.75 as the well-controlled group and those with scores of more than 0.75 as the incompletely controlled group.[12] Comparisons between the 2 groups were performed by chi-square test and Mann-Whitney *U* tests. Multivariate logistic regression model was used to assess the relative associations between the binary outcome (ACQ score $\geq$ 0.75) and a set of covariates. The odds ratios (ORs) with 95% CIs were estimated. The variables with *P* values of less than .05 in the univariate analysis were included in this model. Data were expressed as mean values $\pm$ SD. A *P* value of less than .05 was considered statistically significant.

RESULTS

The study design is shown in Figure 1. A total of 260 patients with AR and asthma were analyzed (Table II). An aggregated ACQ score of 0.75 or more, indicating incomplete asthma control, was found in 108 patients (42%). Patients with incompletely controlled asthma were more likely to be older ($P < .05$), have a lower FEV_1, and higher levels of exhaled NO (all $P < .001$) despite receiving more intensive asthma treatment (daily dose of inhaled corticosteroid and long-acting β2-agonist use) compared with the well-controlled group. The incompletely controlled group was more likely than the well-controlled group (18%) to have moderate/severe persistent AR (44%), but only 50% of the patients had been receiving any rhinitis treatments including leukotriene antagonist, antihistamines, or nasal corticosteroids (NCSs). The well-controlled group was more likely to be taking NCS ($P < .01$). In a multivariate model adjusted by age, asthma therapy, airflow limitation, and FENO, persistence and severity of AR (OR, 2.57; 95% CI, 1.41-4.70; $P < .005$ and