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Subjective cold hyper-responsiveness grade reflects age- and duration-related increase of nonspecific nasal hyperreactivity

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ABSTRACT

Objective: We evaluated the effect of patients' age and duration of allergic rhinitis on nonspecific nasal hyper-reactivity (NHR) using cold dry air (CDA) provocation.
Methods: In 156 patients of various ages with allergic rhinitis and different symptom duration, we evaluated the change of symptoms, the subjective cold hyper-responsiveness (SCH) grade, the change of acoustic parameters such as total nasal volume (TNV) and minimal cross-sectional area (MCA), and the amount of rhinorrhea before and after CDA provocation.
Results: Patients in different age or duration groups did not show significant differences in the change of each nasal symptom. SCH grade 2 or 3 was more frequently observed in patients older than 30 years ($p = 0.018$). There was a significant correlation between the age of the patients and the SCH grade ($R = 0.184$, $p = 0.022$). Patients with >10 years of duration reported higher SCH grade ($p = 0.022$). There was a significant correlation between the duration of disease and SCH grade ($R = 0.284$, $p < 0.001$). However, there were no significant differences in the change of TNV and MCA, and the amount of rhinorrhea after CDA provocation between different age and duration groups.
Conclusion: SCH grade reflects the age- and duration-related increase of NHR. Further studies to elucidate the pathophysiologic mechanisms are needed in the future.

1. Introduction

Nonspecific hyper-reactivity (NHR) is defined as increased responsiveness of the nasal cavity to various commonly encountered, non-allergenic stimuli such as sudden change of temperature or chemical pollutants [1]. A number of protocols have been developed to evaluate such NHR. Direct stimuli (methacholine and histamine) and indirect stimuli (cold air, exercise, and hyperventilation) have been adopted [2], and indirect stimuli are more clinically relevant than direct stimuli [3]. We developed cold dry air (CDA) provocation machinery and proved its usefulness in the evaluation of NHR [4–6].

In patients with allergic asthma, a significant correlation was observed between airway hyper-responsiveness (AHR) and baseline lung function as the duration of disease increased [7]. Also, aging of patients was shown to be related with worse asthma control [8]. These results imply that aging and duration of allergic asthma could influence the emergence of AHR.

Allergic asthma and allergic rhinitis have been viewed not as independent disease entities, but as different spectra of a common allergic disease of a unified airway [9,10]. Based on the concept of 'One airway, one disease', we hypothesized that aging and the duration of allergic rhinitis could also impact the emergence of NHR. Therefore, we evaluated the effect of patients' age and duration of allergic rhinitis on NHR by evaluating the change of allergic symptoms, subjective cold hyper-responsiveness (SCH) grade (which was proved to be useful in evaluating NHR in our previous study) [6], change of acoustic parameters and amount of rhinorrhea between groups of different age and duration of disease.

2. Materials and methods

2.1. Subjects

One hundred and fifty-six patients (99 males and 57 females, 10- to 75-years old) with allergic rhinitis were enrolled. The criteria for inclusion or exclusion are shown in Table 1. By means of skin prick test (SPT) or multiple allegro-sorbent test (MAST), more than 40 kinds of antigens, including mites, fungi, weed or tree pollens, cats, dogs and cockroaches, were tested. Patients were subdivided according to age (from teenager to >50 years of age) and disease duration (from less than 1 year to more than 15

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Table 1
The inclusion and exclusion criteria for the study.

Inclusion criteria
Age: 10–65 years old
Typical symptoms of allergic rhinitis
Strongly positive (more than 3+) to house dust mite
Exclusion criteria
Use of inhaled or systemic corticosteroid within a month
Use of inhaled cromoglycates, astemizole or nedocromil sodium within a month
Inability to stop medication that could affect nasal function
A serious or unstable systemic disease
Pregnant or lactating woman
A history of nasal surgery within 3 months
Nasal polyp or chronic sinusitis proved by plain X-ray or CT of the paranasal sinus
Exposure to chemical irritants
Smoking

MAST: Multiple Allergo-Sorbent Test.

years). We received written informed consent from all patients before their entry into the study, and the study was approved by the Inha University Institutional Review Board Committee on Studies Involving Human Beings.

2.2. CDA challenge

The protocol for CDA challenge has been described previously [4–6]. In brief, the patients were acclimatized to room temperature for 15 min before blowing their nose to remove their nasal secretions; five nasal rinses were then performed with normal saline. About 15 min after humidification, baseline symptom scores for nasal obstruction, rhinorrhea, sneezing and itching were obtained using a visual analogue scale (VAS). The VAS used a 10-cm line with a dot at 1-cm intervals, and the patients marked the severity of their symptoms from 0 to 10 on the line. Patients' degree of subjective cold hyper-responsiveness (SCH) was checked using a previously validated 4-scale SCH questionnaire about their history of discomfort on exposure to cold air (Table 2) [6]. All patients were classified based on the SCH scale, from grade 0 to grade 3. Acoustic parameters such as total nasal volume (TNV) and minimal cross-sectional area (MCA) were obtained by acoustic rhinometry in both nasal cavities. TNV was defined as the volume of the nasal cavity from the nostril to 7 cm deep, and MCA was the smallest dimension of cross-sectional area in the nasal cavity. The method for performing acoustic rhinometry is described elsewhere [11].

Next, the CDA provocation test was performed. Air for medical use was cooled to about 0 °C by passage through a refrigerant air dryer. The cooled air was dried to <10% humidity by passage through a mist separator, and the particles, dust and microorganisms were removed by passage through a filter. CDA was delivered to each patient's nose via a pediatric continuous positive airway pressure mask. The air quality was evaluated by measuring the temperature and relative humidity of air passing through the CPAP mask (Respironics Inc., Murrysville, PA, USA) for 10 min. The patients were instructed to inhale through the nose and exhale through the mouth during the air challenge and to maintain their ordinary breathing frequency and normal breathing pattern. About 400 L of CDA was supplied over 6 min. For the patients' safety, the provocation was stopped immediately in the case of hyperventilation or other major discomfort. However, no patient suffered from major discomfort related to CDA provocation.

Five minutes after provocation, the symptoms were measured again by VAS. TNV and MCA were also obtained in both nasal cavities by repeating the acoustic rhinometry, and the changes were expressed as a percentage. The larger of the values between the right and left nasal cavity was selected. To avoid diurnal variation and inter-test error, all provocations were performed at a fixed time of day by a single experienced examiner. To measure the amount of rhinorrhea, a precision scale with an accuracy of 0.01 g (Mettler, Würzburg, Germany) was used. The examiner measured the weight of several sheets of tissue paper before and after patients blew their nose using that tissue paper.

Table 2
The subjective cold hyper-responsiveness (SCH) questionnaire to predict nonspecific nasal hyper-reactivity.

Q: How great is the discomfort you feel when you are exposed to cold air (for example, when you walk into an air-conditioned room or in the winter)? **A**: (Please check one that is closest to you)			
Absent (grade 0)	Mild (grade 1)	Moderate (grade 2)	Severe (grade 3)
( )	( )	( )	( )

2.3. Statistical analyses

One-way ANOVA and independent *t*-tests were used to compare the change in the symptoms and the TNV and MCA values, and the amount of rhinorrhea between groups. The data is reported as mean ± standard deviation. To compare the proportion of different SCH grades between different age and duration groups, the Chi-square test was used. Linear regression analysis was used to evaluate the correlation between age or disease duration and SCH grade. SPSS 17.0 statistics software (SPSS, Chicago, IL, USA) was used and p values <0.05 were accepted as being statistically significant.

3. Results

Patients in different age or duration groups did not show significant differences in the change of each nasal symptom VAS score (Fig. 1). Comparing the proportions of SCH grade between age groups, patient in their teenage or twenties reported lower SCH grade compared with those in their thirties or older (Fig. 2). Defining the cut-off age group for the significant SCH grade difference, SCH grade 2 or 3 (which reflects the hyper-responsiveness to Cold air) was more frequently observed in patients older than 30 years (Fig. 3a, $p = 0.018$). There was a significant correlation between age and the SCH grade ($R = 0.184$, $p = 0.022$). In terms of disease duration, we found that patients who experienced more than 10 years of symptoms reported a higher SCH grade than those with a shorter symptom period (Fig. 3b, $p = 0.022$). The linear regression analysis revealed a significant correlation between disease duration and SCH grade ($R = 0.284$ and $p < 0.001$).

However, there were no significant differences in the change of TNV and MCA after CDA provocation among different age and duration groups (Fig. 4). Neither were there any significant differences in the amount of rhinorrhea between groups (Fig. 5).

4. Discussion

In our study, there were no significant differences in the changes of each nasal symptom measured by VAS. However, the proportion of patients with SCH grade 2 or higher increased significantly as age and disease duration increased. VAS scores for nasal obstruction, rhinorrhea, sneezing and itching are rather nonspecific symptoms, in that patients with any kind of rhinitis could suffer from those complaints. However, the SCH grade measures more specific discomfort when patients are exposed to cold air. Therefore, the SCH grade could be a more suitable attribute for evaluating NHR. As we proved the usefulness of SCH