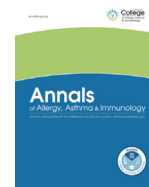




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Autonomic function in adults with allergic rhinitis and its association with disease severity and duration

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ABSTRACT

Background: The association between allergic rhinitis (AR) and the autonomic nervous system (ANS) has recently received substantial attention. However, no studies have assessed how the heart rate variability (HRV) parameters are associated with duration and disease severity in AR.

Objective: To compare the difference in autonomic conditions among individuals with AR of various durations and severities and healthy controls.

Methods: We divided individuals with AR into subgroups based on duration and severity of disease. Next, we measured HRV, and the results were compared among subgroups and healthy controls.

Results: High frequency (HF) and normalized high frequency (NHF) were significantly higher in the intermittent group than in the control group, whereas normalized low frequency (NLF) and the ratio of absolute LF to HF power (LF/HF) were significantly lower in the intermittent group than in the control group. Furthermore, NLF was significantly higher in the persistent group than in the intermittent group. HF and NHF were significantly higher in the mild group than in the control group, whereas NLF and LF/HF were significantly lower in the mild group than in the control group. The total nasal symptom and itchy nose scores were negatively correlated with NHF.

Conclusion: Our results indicate that patients with intermittent and mild AR have hypervagal activity and hyposympathetic activity, and the predominance lessens in patients with more persistent AR and severe symptoms. Further investigation of the mechanisms underlying the association between autonomic function and persistent and severe AR is needed.

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Introduction

Allergic rhinitis (AR) is an inflammatory disease of the nasal membranes characterized by symptoms such as nasal congestion, rhinorrhea, nasal itching, and sneezing.¹ According to the Allergic Rhinitis and its Impact on Asthma (ARIA) classification, the condition is classified as either mild or moderate to severe and as either intermittent or persistent, depending on symptom severity and duration of symptoms.² In South Korea, the mean (SD) prevalence of AR is 16.2% (1.0%), and this value tends to decrease with age.

According to the ARIA classification, 76.1% of AR cases are intermittent, whereas 23.9% are persistent; meanwhile, 67.2% are mild and 32.8% are severe.³

It has been proposed that autonomic nervous system (ANS) dysfunction is an important factor underlying AR. For instance, 2 case-control studies reported a higher rate of parasympathetic predominance in patients with AR than in healthy controls.^{4,5} Another study investigated the association between ANS function and AR severity in children; the researchers assessed ANS activity using the sympathetic skin response and R-R interval variation. The results indicate that vagal hyperactivity increased with AR severity.⁶ Conversely, a more recent study reported that patients with seasonal AR have parasympathetic hypoactivity when compared with healthy controls.⁷

Several methods can be used to evaluate the the ANS; researchers can measure sympathetic skin response, R-R interval variation, and heart rate variability (HRV). Among these, HRV is a noninvasive and quantitative tool that can be used to evaluate the

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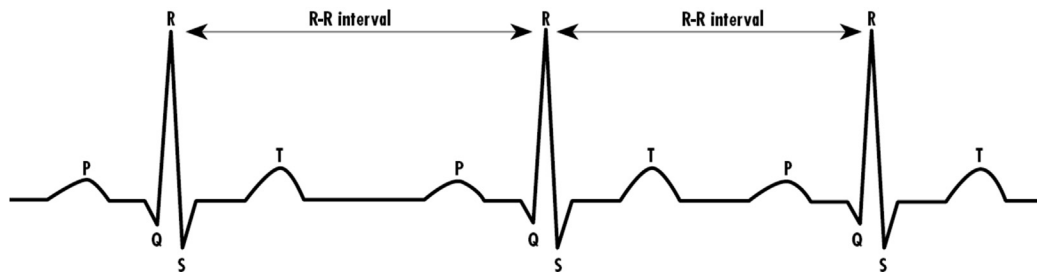


Figure 1. R-R interval and heart rate variability. R-R interval is the time between heartbeats. Heart rate variability analysis is an analysis of variations in the interval between heartbeats based on time and frequency domain.

function of both the sympathetic and parasympathetic branches of the ANS (Fig 1).⁸

However, no studies have assessed how the HRV parameters are associated with duration and disease severity in AR. Therefore, the aims of this study were to compare ANS function among healthy controls and AR subgroups that were classified according to the ARIA guidelines and to investigate the influences of various clinical symptoms on ANS function in patients with AR.

Methods

Patients With AR

A total of 35 patients were recruited from the Department of Otorhinolaryngology of Korean Medicine at Kyung Hee University Hospital at Gangdong between March 12 and April 17, 2013. The inclusion criteria were as follows: (1) age older than 18 years; (2) presence of AR symptoms, such as clear nasal discharge, nasal obstruction, itchy nose, and sneezing; and (3) diagnosis of allergy using the skin prick test. The exclusion criteria were as follows: (1) presence of rhinosinusitis, nasal polyposis, or neoplasm on nasal endoscopy; (2) treatment using asthma medication or antihistamines within 2 weeks, corticosteroids within 1 month, or a nasal/oral decongestant or leukotriene receptor antagonist within 1 week; (3) presence of any disease known to affect HRV (eg, cardiovascular, endocrinologic, autoimmune, neurologic, or psychiatric disorder, including alcoholism and polytoxemia); (4) history of smoking; (5) anticholinergic, antidepressant, or contraceptive pill use for at least 4 weeks before the study; (6) use of hormone replacement therapy; or (7) pregnancy.

Written informed consent was obtained from all patients before enrollment. This study was approved by the Institutional Review Board of Kyung Hee University Hospital at Gangdong.

Healthy Controls

The control group comprised healthy people who were recruited from the Department of Sasang Constitutional Medicine, Kyung Hee University Korean Medicine Hospital, between November 2014 and March 2015. All participants were healthy, Korean individuals older than 18 years. They had undergone a general health checkup (recording of disease history, physical examination, vital signs, and chest radiography) and laboratory tests (measurement of complete blood cell count, total serum IgE, aspartate transaminase, alanine transaminase, blood urea nitrogen, creatinine, and erythrocyte sedimentation rate) and had no abnormal findings. The exclusion criteria were as follows: (1) presence of any disease known to affect HRV (eg, allergic, cardiovascular, endocrinologic, autoimmune, neurologic, or psychiatric disorders, including alcoholism and polytoxemia); (2) history of smoking in the 3 months before the study; and (3) pregnancy or lactation. After screening the healthy controls, we randomly

extracted 32 individuals who were equally matched to the age and sex distributions of the AR group.

Skin Prick Test

The skin prick test was performed according to a routine procedure. Eleven common aeroallergens (*Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, dog fur, cat fur, grass mixture, tree mixture, mugwort, ragweed, *Alternaria tenuis*, *Aspergillus fumigatus*, and cockroach) were used (Allergopharma GmbH & Co KG, Reinbeck, Germany). The skin prick test was performed on the volar surface of the forearm; negative (50% glycerin saline) and positive (0.1% histamine phosphate) controls were also used. The results were examined at 15 minutes, and the resultant wheals and flares were measured. A test result was considered positive if the diameter of the wheal was the same or larger than that of the positive control wheal.⁹ Skin prick tests were not performed on the healthy controls.

AR Subgroups and Evaluation of Nasal Symptoms

Patients with AR who met the inclusion criteria were classified, according to the ARIA criteria, as having either intermittent AR (IAR; <4 days per week or <4 weeks per year) or persistent AR (PAR; >4 days per week and >4 weeks per year); AR was also categorized as either mild (symptoms were present but did not interfere with quality of life) or moderate to severe (symptoms were serious enough to interfere with quality of life).² Nasal symptoms (ie, rhinorrhea, nasal obstruction, itchy nose, and sneezing) were assessed using a 4-point Likert scale (0 indicating no symptoms; 1, mild; 2, moderate; and 3, severe). The total nasal symptom score (TNSS) was calculated as the sum of separate symptom scores and ranged from 0 to 12.

HRV Analysis

All patients with AR, as well as the healthy controls, were assessed using the same procedure and equipment. They removed any metal attachments from their bodies, were seated on comfortable chairs in a quiet room, and were asked to relax for 15 minutes. After the relaxation period, electrocardiography was performed for 5 minutes (SA-3000P, Medicore Inc, Seoul, Korea). Because HRV reflects the activity of the ANS on the sinus node, abnormal heartbeats and artifacts were excluded from the electrocardiographic recordings to obtain more reliable results.¹⁰ HRV was assessed on the basis of frequency domain measurements performed using fast Fourier transformation.^{8,11} All HRV parameters used in this study were logarithmically transformed to correct the skewness of distribution (Table 1).

Statistical Analysis

No report has compared autonomic function using HRV among AR subgroups that were classified according to ARIA guidelines. In a

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