Otolaryngology–Head and Neck Surgery (2007) 136, 51-56

ORIGINAL RESEARCH

Autonomic nervous system evaluation in allergic rhinitis

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OBJECTIVES: To evaluate the relationship between allergic rhinitis (AR) and autonomic nervous system (ANS) dysfunction.
METHODS: Quantitative ANS testing was completed in 10 patients with AR confirmed by clinical findings and allergy testing. This data was compared to 16 age-matched controls.
RESULTS: ANS scores were significantly abnormal in AR patients when compared to normal controls. The composite autonomic scale score for the AR group was significantly impaired when compared to controls (1.6 vs 0.63, $P < 0.0001$). Additionally, subscore values quantifying the level of dysfunction within the sympathetic nervous system (1.0 for sudomotor and 0.5 adrenergic) were found to be significantly different ($P < 0.0001$ and 0.018). The mean subscore value quantifying the level of dysfunction within the parasympathetic system (cardiovagal) was not found to be significantly different from controls ($P = 0.38$).
CONCLUSIONS: ANS dysfunction, specifically sympathetic hypofunction, was identified in all of the allergic rhinitis patients studied. Further characterization of the type of ANS abnormality may allow the development of novel pharmacologic therapies for these disorders.

Allergic rhinitis (AR) is estimated to affect 20 to 40 million U.S. residents and results in over 10 million physician outpatient visits annually, resulting in total indirect and direct costs of $2.4 to $4 billion annually.[1] Extensive research has been done concerning the pathophysiology of this disorder and most of it has centered on the IgE-allergen relationship and the release of inflammatory mediators, notably histamine. However, not all of the symptoms or signs of AR can be explained solely by this IgE-mediated mechanism. Autonomic nervous system (ANS) dysfunction has been proposed as a contributory factor.[2]

The classical symptoms of the nasal allergic response include nasal itching, sneezing, rhinorrhea, and nasal congestion in response to seasonal or perennial stimuli such as dust mites, pet dander, mold, and pollen.[3] Some patients with chronic rhinitis complain of these same symptoms in response to nonallergic stimuli such as cold air, tobacco smoke, and other irritants.[4] Approximately half of chronic rhinitis patients are classified as having AR and half suffer from nonallergic rhinitis, including vasomotor rhinitis (VR).[5] There are no specific symptoms that differentiate patients with AR from those with VR; however, specific questioning with regard to the inciting physical, environmental, and emotional stimuli can be used to distinguish between them. AR can be diagnosed by provocative exposure along with identification of the type I hypersensitivity reaction, while the symptoms of VR typically occur in response to specific physical stimuli (eg, cold air, temperature change, fatigue, anxiety).[6,7]

While ANS dysfunction, particularly sympathetic hypofunction, has been recently described in patients with nonallergic rhinitis, ANS function in AR patients has not been

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Supported by a grant from the American Academy of Otolaryngic Allergy.

Presented at the Annual Meeting of the American Academy of Otolaryngic Allergy, Los Angeles, CA, September 22-25, 2005.

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0194-5998/$32.00
doi:10.1016/j.otohns.2006.08.014

systematically characterized. The purpose of this study is to quantify and characterize ANS function in patients with AR utilizing a state-of-the-art ANS testing laboratory.

METHODS

This study was approved by the Institutional Review Board of the Medical College of Wisconsin (MCW). Patients who consented to participate in the study were recruited from the MCW Otolaryngology and Allergy clinics between January 1 and December 31, 2004. Recruitment was based on diagnostic criteria defining perennial AR including at least nine months of specific symptoms including nasal obstruction, nasal itching, sneezing, and clear secretions with exacerbations related to environmental and/or occupational exposure. Additional criteria included an absence of sinus infection in the previous four months, physical findings such as mucous membrane swelling and thickening on endoscopic sinonasal examination, and positive allergy evaluation via skin prick testing.

Historical control subjects were between the ages of 18 and 50 and had no historical or physical evidence of paranasal sinus inflammatory disease. In addition, smokers, subjects with a history of cardiovascular disease or antihypertensive medication usage, and pregnant patients were excluded as controls.

Exclusion criteria for test subjects included: subjects younger than 18 or older than 79 years, smokers, subjects with a history of cardiovascular disease, patients on antihypertensive medications, or pregnant patients. In addition, patients with a diagnosis of AR who had been medically treated for these disorders in the last two months were excluded, as were patients with acute rhinosinusitis, nasal polyposis, and neoplasms noted on nasal endoscopy. All subjects underwent a complete physical examination and a detailed medical history with special attention given to sinonasal/allergy signs and symptoms. All subjects underwent the following battery of tests to further characterize and quantify their sinonasal and allergic disease.

Allergy Evaluation

All subjects underwent percutaneous and intracutaneous allergy skin testing. These techniques utilize the introduction of an allergen into or under the dermis. After a suitable time period, the size of the resultant wheal and flare reaction is measured to assess the patient's sensitivity. The determination of allergic rhinitis was then made after correlating skin test results with patient history. A wheal diameter of greater than 3 mm was considered a positive skin test. This is done routinely to evaluate allergy status at our institution.

Sinonasal Evaluation

All subjects underwent sinonasal endoscopy. In this procedure the nose and sinuses were evaluated with 0-degree or 30-degree rigid nasal endoscopes. This was done as part of the routine diagnostic work-up for chronic sinonasal disease and was used to exclude concomitant disease (ie, acute rhinosinusitis, nasal polyposis, and neoplasms).

Autonomic Nervous System Evaluation

In preparation for this testing, anticholinergic medications were discontinued for 48 hours, vasodilatory drugs were stopped for 24 hours, and caffeine and tobacco were held for 8 hours prior to testing. ANS testing consists of the following five noninvasive tests:

1) The quantitative sudomotor axon reflex test (Q-SART) was performed at the foot, distal leg, proximal leg, and forearm to measure postganglionic sudomotor function. The patient rested supine in a comfortably warm room. A small multi-compartmental sweat capsule was placed on the extremity and a 2-mA constant electrical current stimulus was used for iontophoresis of 10% acetylcholine solution to trigger sweating. Nitrogen gas was then sent through high- and low-pressure regulators, through the sudometer, through the sweat capsule, and back through the sudometer. Sweat output (uL/cm^2) was recorded, compared with normal controls, and analyzed for side-to-side differences.
2) Heart rate response to deep breathing was quantified next. The patient was instructed to practice breathing deeply with inspiratory and expiratory cycles of five seconds each. Heart rate was then recorded using an electrocardiogram (ekg) monitor. The patient took deep breaths in and out for eight cycles of 10 seconds. The R-R interval was then converted to heart rate and the mean of the five largest consecutive responses was used to get the heart rate range. This was performed twice and the best response was recorded.
3) The heart rate and blood pressure responses to the Valsalva maneuver were assessed using an EKG monitor and a continuous blood pressure monitor (Finapres, Englewood, CO). The patient blew into a tube connected to a manometer and maintained a pressure of 40 mm Hg for 15 seconds, giving the patient the sensation of lifting weights. The heart rate and blood pressure were recorded and analyzed. The Valsalva ratio was calculated by taking the ratio of the longest R-R interval. This ratio was compared to known age-adjusted normal subjects. The better of two responses was used.
4) Blood pressure and heart rate responses to upright tilt were determined. The patient rested quietly in the supine position on the tilt table for at least five minutes with the EKG monitor and continuous blood pressure monitor cuff in place. Heart rate and blood pressure were recorded at baseline and continuously while the patient was tilted upright and maintained in this position for five minutes. The patient was then tilted back and the response was monitored for three additional minutes.
5) The thermoregulatory sweat test involved placing the patient in a sauna-like room with a temperature of 120°F to 130°F and 28% to 35% humidity. The patient's fore-