The role of allergic rhinitis in nasal responses to sudden temperature changes

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Background: Air conditioning–induced rhinitis in allergic individuals is a common epidemiologic finding, but its physiopathology is still controversial. The aim of this study was to describe and compare the effects of experimental air conditioning temperature changes on the nasal mucosa of individuals with persistent allergic rhinitis compared with a control group.

Methods: A case-control challenge study was performed in a laboratory of thermal comfort with experimental twin challenge chambers set at a 12°C difference in temperature. A group of 32 patients with persistent allergic rhinitis and a group of 16 control subjects were exposed for 30 minutes, 3 times alternately in each chamber. Nasal symptom scores were recorded and nasal samples collected before, immediately after, and 24 and 48 hours after the challenge.

Results: The rhinitis group showed a higher symptom score, epithelial shedding, percentage of eosinophils, total inflammatory cells, leukotriene C_4, eosinophil cationic protein, albumin, and tryptase levels compared with controls. There was also a significant increase in symptom score, total cells recovered, percentage of eosinophils, epithelial shedding, albumin, myeloperoxidase, and soluble intercellular adhesion molecule 1 in both groups compared with baseline levels.

Conclusion: Sudden temperature changes led to a more pronounced inflammatory nasal response in the rhinitis group with the recruitment and activation of eosinophils.

Clinical implications: Persistent allergic rhinitis is a risk factor for developing sudden temperature change–related rhinitis even in the absence of allergen exposure. (J Allergy Clin Immunol 2006;118:1126-32.)

Key words: *Indoor air quality, environmental illness, air conditioning, inflammatory mediators*

Abbreviations used

ECP: Eosinophil cationic protein
IAQ: Indoor air quality
LT: Leukotriene
PAR: Persistent allergic rhinitis
sICAM-1: Soluble intercellular adhesion molecule 1

Indoor air quality (IAQ) is rapidly gaining importance as a public health issue worldwide, as urban society spends progressively more time indoors. IAQ-related problems are reported in various climatic conditions including tropical climates,[1] and are considered the most common environmental health issue faced by clinicians.[2] The factors associated with IAQ have a complex interaction and include temperature, humidity, air exchange rates, exposure to organic and inorganic indoor air pollution, odors, air movement, and work and psychosocial factors. The changes in the work pattern of the new office environment are characterized as dynamic, with interactive project teams and different or shared workplaces.[3] This increased movement can lead to increased exposure to different indoor and outdoor conditions with wide range and sudden temperature changes. The presence of air conditioning systems[1,4,5] and atopic phenotype[6-8] are risk factors consistently associated with mucosal symptoms in IAQ epidemiologic studies. Interestingly enough, most studies do not find causal allergen exposure in nonresidential and nonindustrial settings.[9-11]

Allergic rhinitis is clinically defined as a symptomatic disorder of the nose induced by an IgE-mediated inflammation after allergen exposure of the membranes lining the nose. Symptoms of rhinitis include rhinorrhea, nasal obstruction, nasal itching, and sneezing, which are reversible spontaneously or with treatment. Allergic rhinitis is a global problem affecting 10% to 25% of the population and can be subdivided into intermittent or persistent disease according to the frequency of the symptoms.[12] Allergen exposure is the most potent trigger of nasal symptoms, but the nasal mucosa of the allergic population has a lower threshold to various stimuli.[13] Considering that cold and dry air can induce mast cell degranulation in individuals with allergy,[14] the role of air conditioning–related sudden temperature changes per se in the atopic population remains to be elucidated. The aim of the current study was to induce experimental sudden temperature

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changes to describe possible symptoms and inflammatory changes in the nasal mucosa of individuals with allergy compared with controls.

METHODS

Selection of individuals

After the authorization of the ethics committee of the State University of Sao Paulo (Protocol 930/02), 48 individuals who signed a consent form were selected out of patients with allergy and healthy individuals. The participants in the study ranged in age from 20 to 45 years and were not undergoing treatment for endocrine, infectious, or rheumatologic diseases. They underwent a medical history, physical examination, and skin prick testing with standardized allergens. The tests were performed in duplicate with epicutaneous puncture and evaluated after 20 minutes according to a standard procedure. Tests were considered positive for allergen sensitization with mean arithmetic papules larger than 4 mm for allergens. Individuals with positive reactions to saline or negative reactions to histamine were excluded. The case group consisted of 32 individuals, 22 men and 10 women who had allergic rhinitis (nasal pruritus, aqueous nasal discharge, sneezing, and nasal blockage) and positive cutaneous tests for at least 1 allergen (*Dermatophagoides pteronyssinus*, *Blomia tropicalis*, *Aspergillus fumigatus*, *Alternaria alternata*, dog and cat epithelium, 10 mg/mL histamine and saline (ASAC PHARMA, International Pharmaceutical Immunology, Alicante, Spain). All patients from the rhinitis group were classified as persistent allergic rhinitis (PAR) according to the Allergic Rhinitis and its Impact on Asthma study criteria.[12] The control group was composed of 8 men and 8 women without history or symptoms of allergic diseases and who had negative tests for allergic diseases, age-matched with the case group. Another group of 6 individuals with PAR not exposed to temperature changes was used to address the variance in the results because of nasal sampling and natural variation in nasal epithelium in allergic rhinitis. Individuals with evidence of viral illnesses, immunologic impairment, or use of any antihistamine or anti-inflammatory medication 14 days before temperature tests were excluded.

Temperature tests

The selected population dressed in standardized thermal protection of 1.0 clothing units (CLO).[15] Temperature tests were conducted in twin isolated chambers controlled for temperature, humidity, sound, light, and ventilation. The chambers had exclusive air supply from a fan coil with a nominal output of 340 m^3/h and a chiller with a capacity of 5 tons of refrigeration. The experimental system supplied air exchange rates of more than 27 m^3/h/person, which assured carbon dioxide levels in the chambers of less than 700 parts per million. Individuals were introduced into separate chambers for temperature challenges. The 2 chambers had a temperature difference of 12°C or 26.6°F, where the warm chamber was 26°C (78.8°F) and the cold chamber 14°C (57.2°F), both with the relative humidity of the indoor air set at 60% ± 2%. After 30 minutes of acclimatization, individuals were asked to move from one chamber to the other. All participants completed arbitrarily chosen 3 rounds of temperature changes totaling 3 hours of challenge and after final acclimatization were re-examined and submitted to nasal sampling before, immediately after, and 24 and 48 hours after challenge.

Clinical evaluation

All participants had a medical history taken and were given a physical examination to complete the Meltzer Modified Rhinitis Score.[16,17] In brief, symptoms of nasal pruritus, nasal drip, nasal blockage/sneezing, and post nasal drip and physical findings of rhinorrhea, inferior turbinate edema, inferior turbinate appearance, and oropharyngeal alterations were quantified on a scale of 0 to 3 for each item, with a maximum total score of 24 points.

Nasal samples were obtained before, immediately after (4 hours), and 24 and 48 hours after beginning the challenge. Nasal samples were obtained by using nasal brushes with gentle rotational movement on the superior part of both inferior turbinates for 30 seconds according to a previously described technique.[18] Samples were diluted in 5 mL PBS. Afterward, samples were centrifuged in a refrigerated centrifuge at 170*g* for 10 minutes. Aliquots of the supernatants were frozen at –80°C. The cell pellet was resuspended in 1 mL PBS. One volume of a solution containing 0.5% crystal violet dissolved in 30% acetic acid was added to 9 volumes of the cell suspension. The total cell number was determined by counting in a hemocytometer. Differential cell counts were performed after cytocentrifugation and staining with hematoxylin/eosin (Hema 3, Fisher Scientific Company, Swedesboro, NJ).

Inflammatory mediators

The levels of the following mediators were measured in cell-free supernatants of nasal samples:

- Leukotriene (LT) C_4 and histamine were assayed by using commercially available ELISA kits (Cayman Chemical Co, Ann Arbor, Mich). Detection limits were 10 pg/mL and 0.5 nmol/L, respectively.
- Soluble intercellular adhesion molecule 1 (sICAM-1) levels were determined by using an ELISA kit (R&D Systems, Abingdon, United Kingdom) with a detection limit of 0.35 ng/mL.
- Tryptase and eosinophilic cationic protein (ECP) were determined with commercially available assays (Pharmacia CAP System, Uppsala, Sweden) according to the manufacturer's instructions. Detection limits were 2 μg/L for the ECP and 1 μg/L for the tryptase.
- Albumin was measured by means of nephelometry (N Antiserum anti-Albumin, Dade Behring, Deerfield, Ill), with a detection limit of 1.4 mg/L.

Myeloperoxidase activity in cell lysates was quantified by changes in absorbance (OD 460 nm) resulting from decomposition of H_2O_2 in the presence of orthodianisidine.[19]

Levels of indoor pollution

Indoor air was monitored for the following:

- Viable fungal spores. Samples were collected with a 6-stage Andersen sampler (Andersen Samplers Inc, Atlanta, Ga), and Sabouraud dextrose agar (Acomedia, Baltimore, Md) Petri dishes with 10 μg/mL of agar sabouraud dextrose with chloramphenicol were used for the culture, identification, counting, and measurement of airborne fungal spores.
- Particulate matter, using the manual gravimetric method (Handi-Vol, Rio de Janeiro, Brazil) and laser particle counter (Hand-Held 3016, Lighthouse, Tulsa, Okla).
- Carbon dioxide levels in parts per million (CO_2 monitor 535, Testo, Hamburg, Germany).

Statistical analysis

Cell count for each cell type was expressed as percentage of total cells. Differences among groups and time were examined by ANOVA repeated measures to compare group differences (group effect) and to compare variations in time after the challenge (time effect) in both groups. These results were investigated in depth using post hoc comparisons (Newman-Keuls test). Previous results from a study of 17 cases and 16 controls showed a minimum difference between groups of 9.23% among all variables studied. A 2-tailed *t* test was used for power calculation, indicating that 32 individuals with