

LETTER TO THE EDITOR

**NARES PATIENTS HAVE MORE RESPIRATORY INFECTIONS
THAN ALLERGIC SUBJECTS**M. CASSANO¹, P. CASSANO¹, F. MORA² and G. CIPRANDI³¹*Department of Otolaryngology, University of Foggia;* ²*ENT Clinic, University of Genova;*³*Azienda Ospedaliera Universitaria San Martino, Genova, Italy**Received December 12, 2010 – Accepted July 13, 2011*

Respiratory infections (RI) represent a frequent challenge for physicians. Allergic patients could present higher susceptibility to contract RI than non-allergic subjects. Non-allergic rhinitis with eosinophils (NARES) has been little investigated. This preliminary study was performed to evaluate the number and duration of RI and their sequelae in NARES and allergic patients, and non-allergic healthy subjects. Forty healthy non-allergic subjects (22 males, mean age 29 years), 40 patients with allergic rhinitis (AR) (19 males, mean age 35), and 40 NARES patients (18 males, mean age 34) were evaluated. The considered parameters were: nasal eosinophils, total number, duration in days of RI, and RI severity. NARES patients had more eosinophils than AR patients and normal controls ($p<0.01$); RI duration was longer in NARES patients than in AR ones ($p<0.05$) and controls ($p<0.01$); RI were more severe in NARES patients than in AR ones ($p<0.05$) and controls ($p<0.01$); pneumonia and asthma were more frequent in both NARES and AR patients than controls ($p<0.05$ and $p<0.01$). In conclusion, this preliminary study shows that NARES may induce more severe respiratory infections than allergic rhinitis.

Respiratory infections (RI) are a frequent challenge for physicians (1). Allergic rhinitis (AR) patients have typically Th2-polarization and reduced Th1-response. Interferon-gamma, a Th1-derived cytokine, is deputized for fighting infections. Allergic patients could therefore present higher susceptibility to contract RI than non-allergic subjects (2). In addition, treatments with drugs able to reduce allergic inflammation diminished both the number and severity of RI in allergic patients (3). In other words, the high susceptibility to infections in allergic patients may reverse after treating allergic reactions. Moreover, RI represent a social problem both for the pharma-economy and the impact on the social milieu of the subject. Non-allergic rhinitis

with eosinophils (NARES) is a disease characterized by mucosal inflammation with typical abundant eosinophilic infiltrate and nasal symptoms similar to those of AR but without sensitization (4). This nasal disorder, despite being well known, has been little investigated. Therefore, this preliminary study was carried out to evaluate the number and duration of RI and their sequelae in NARES, allergic and non-allergic healthy subjects.

MATERIALS AND METHODS

The patients were evaluated between September, 2009 and June, 2010: 40 healthy non-allergic subjects (22 males, mean age 29 years), 40 AR patients (19 males,

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mean age 35), and 40 NARES patients (18 males, mean age 34).

Inclusion criteria were: diagnosis of AR or NARES, presence of typical symptoms, history of previous RI, sensitization to perennial allergens (such as house dust mites or pets) in AR patients. Exclusion criteria were: current use of nasal corticosteroids (they had to have been withdrawn at least 1 month prior to recruitment), severe systemic disorders, immune deficiency, and active smoking. The review board approved the study.

AR was diagnosed on the basis of typical history of nasal-ocular symptoms and positive skin prick test (5). NARES was diagnosed on the basis of typical history of nasal-ocular symptoms, eosinophilic infiltrate >5%, and negative skin prick test (4). RI were clinically diagnosed as previously reported (2). Briefly: the investigator diagnosed RI on the basis of the symptoms recorded by the patient on a study diary card and counted the number of episodes. The diagnosis of RI was made when at least 2 symptoms or fever (axillary temperature $\geq 38^{\circ}\text{C}$) were present for at least 48 hours besides one other symptom. The symptoms taken into consideration for diagnostic purposes were: mucopurulent rhinorrhea (stuffy and/or dripping nose), sore throat, cough (dry or productive), otalgia (earache), fever, dyspnoea, and mucopurulent secretion.

The considered parameters were: nasal eosinophils (% of recovered cells by scraping), total number and duration in days of RI, RI severity assessed by Visual Analogue Scale (VAS), total number of lower airways infections and asthma attacks in the three groups.

Data are expressed as mean and standard deviation; Kruskal-Wallis and Wilcoxon tests were used.

RESULTS

Table I shows the findings: NARES patients

had more eosinophils than AR patients and normal controls ($p<0.01$); RI duration was longer in NARES patients than AR ones ($p<0.05$) and controls ($p<0.01$); RI were more severe in NARES patients than in AR ones ($p<0.05$) and controls ($p<0.01$); pneumonia and asthma were more frequent in both NARES and AR patients than controls ($p<0.05$ and $p<0.01$).

DISCUSSION

This preliminary study demonstrates that both NARES and allergic subjects may have more numerous, prolonged and severe RI than non-allergic subjects. These findings confirm previous reports on allergic patients (2, 6). In addition, NARES and AR patients may have more numerous RI sequelae, such as lower airways infections and asthma attacks, than non-allergic healthy subjects. These findings underline the role of nasal disorders as risk factors for lower airways diseases as pointed out by ARIA guidelines (5).

However, this study provides the first evidence that NARES patients may have more prolonged and severe RI than allergic patients. A possible explanation might be due to the more intense nasal inflammation present in NARES patients. In fact, it is well known that eosinophils are more abundant in NARES than in AR (7-10). Eosinophils are very relevant inflammatory cells, as they release several pro-inflammatory cytokine and toxic basic proteins (4). Therefore, a more intense nasal inflammation might allow more severe infections and sequelae.

On the other hand, these results have to be

Table I. Mean $\pm$ SD of nasal eosinophils, number and duration of RI, total cases of lower airways infections and asthma attacks in: NARES patients, allergic patients and healthy controls.

	NARES patients	Allergic patients	Normal controls
Nasal Eosinophils %	10.3 $\pm$ 2.6	4.7 $\pm$ 1.2	0.2 $\pm$ 0.3
Total RI number	3.1 $\pm$ 0.4	2.8 $\pm$ 0.6	2.6 $\pm$ 0.4
Total RI duration (days)	11.6 $\pm$ 3.1	7.8 $\pm$ 2.2	4.7 $\pm$ 1.7
Symptom severity (VAS)	9.1 $\pm$ 0.6	6.7 $\pm$ 1.0	4.3 $\pm$ 0.8
Lower Airways infections	14	11	4
Asthma attacks	21	16	0

considered preliminary as further studies should be conducted to verify these hypotheses. An increased number of subjects and a longer period of observation must be observed. In spite of these limits, the present findings underline the importance of the eosinophilic inflammation as a crucial factor involved in the response to infectious diseases.

In conclusion, this preliminary study provides the information that NARES may induce more severe RI than AR, although this issue should be better investigated.

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