

NASAL EOSINOPHILS CORRELATE WITH FEV₁ IN PATIENTS WITH PERENNIAL ALLERGIC RHINITIS ASSOCIATED TO ASTHMA

G. Ciprandi (1), M. Milanese (2), M.-A. Tosca (3),
I. Cirillo (4), A. Vizzaccaro (4), V. Ricca (5)

SUMMARY

Background: Eosinophil inflammation is present in nasal and bronchial mucosa and a clear link between upper and lower airways exists. Our aim was to evaluate whether nasal inflammation correlates with lung function in patients with perennial allergic rhinitis associated with asthma.

Methods: Eighty perennial allergic rhinitics with mild asthma, aged from 18 to 46 years, were enrolled. Nasal scraping and spirometry were performed in all subjects.

Results: A close relationship between the nasal eosinophil number and the percentage of predicted FEV₁ was demonstrated ($r = -0.76$; $p < 0.0001$).

Conclusions: Nasal cytology may be considered a non-invasive tool to assess airway inflammation in mild asthmatics with associated allergic rhinitis.

Key-words: Perennial allergic rhinitis - Mild asthma - Nasal eosinophils - FEV₁.

INTRODUCTION

Allergic rhinitis and asthma frequently coexist in the same patient and a clinical relationship between allergic rhinitis and asthma has been defined for a long time (1). Thus, an increasing body of evidence suggests the existence of a clear link between upper and lower airways (2, 3).

Epidemiological data support the connection between allergic rhinitis and asthma. We previously reported that 77% of conscripts with allergic rhinitis suffered from asthma (4). Anatomical connections between allergic rhinitis and asthma are widely reported (5). The immunopathological features of allergic rhinitis and asthma are substantially similar: there is an inflammatory infiltration, including Th2 cells, mast cells, and eosinophils (6). Mediators, such as histamine and leukotrienes, are demonstrated both at nasal and bronchial level in rhinitics and asthmatics (7). The cytokine pattern is typically characterized by a Th2 polarization in both disorders (8).

However, importantly, vascular tissue and smooth muscle characterize the final response, i.e. nasal

congestion and bronchospasm, respectively. For this reason antihistamines and antileukotrienes can be used in both diseases, although with different efficacy. Nevertheless, control disease drugs, i.e. topical corticosteroids, are highly useful in both diseases (9, 10).

Asthma is defined pathologically as a chronic inflammation of the lower airways (10), but also allergic rhinitis is characterised by an inflammatory infiltration of the upper airways (11). The concept of "one-airway one disease" is now widely accepted (2, 3).

However, when evaluating bronchial inflammation, bronchoscopy cannot be recommended as routine examination and induced sputum has been proposed for this aim. On the other hand, nasal cytology is a technique that allows some advantages: easy to be performed, economic, non-invasive, and repeatable many times in the same patient.

The aim of our study was to investigate whether a relationship can be demonstrated between nasal inflammation and lung function in allergic rhinitics with concomitant asthma.

MATERIALS AND METHODS

■ **Subjects:** Fifty-two women and twenty-eight men were enrolled. Their age ranged from 18 to 46 years (mean 33.4 yrs). All patients suffered from rhinitis and

(1) Allergologia e U.O. ORL - Dipartimento Testa Collo - Ospedale San Martino - Genova.

(2) Pneumologia - Ospedale S. Corona - Pietra Ligure (SV).

(3) Istituto Giannina Gaslini - Genova.

(4) Ospedale Marina Militare - Dipartimento Medicina - La Spezia.

(5) ASL 3, Torino (Italy).

were sensitized to house dust mite, cat, or dog allergens. The diagnosis of perennial allergic rhinitis was made on the basis of the concordance between history and positive skin prick test for perennial allergens as described elsewhere (4). Patients were included in the study also on the basis of a clinical history of asthma and an historical reversibility of airway obstruction of at least 12% of FEV₁ from baseline.

Subjects with allergy to pollens, acute upper respiratory infection and use of antibiotics, intranasal or oral corticosteroids, antileukotrienes, and antihistamines within the previous 4 weeks were excluded. No subject received long-acting β 2-agonists during the previous month. None of the patients was an ex or a current smoker.

The study was approved by the Institutional Review Board and an informed consent was obtained from all patients.

■ **Nasal cytology:** Nasal specimens for cytology were obtained by scraping the head of the inferior turbinate with a cotton swab, as described in previous report (12). Briefly, after the nasal scraping, the cotton tip of the swab was immersed in a plastic tray with phosphate-buffered saline (PBS) and transferred to a 10 mL polypropylene tube. The recovered fluids were centrifuged at 220 g for 10 minutes, and each pellet was re-suspended in PBS (2 mL). Cell suspensions were filtered to reduce the quantity of mucus, and cytospin slides were prepared by using standard techniques. Smears were stained with Diff Quik stain and were analysed by optic microscope (Olympus U-SPT, Olympus Italy, Rome). Eosinophil numbers were expressed as a mean of 10 optical fields at 100x magnification. Samples were examined in a blinded fashion by the same observer (VR).

■ **Sensitizations:** They were assessed by skin prick test, as stated by the Italian Society of Allergy and Clinical Immunology (13). The allergen panel consists of: mites (*Dermatophagoides farinae* and *pteronyssinus*), cat, dog, grass mix, *Compositae* mix, *Parietaria Officinalis*, birch, hazel tree, olive tree, *Alternaria Tenuis*, *Cladosporium*, *Aspergilli* mix (D (DHS-Bayer Group, Milan, Italy).

■ **Lung function:** Spirometry and flow-volume curves were obtained by using a computer-assisted spirometer (COSMED, Eurasem, Italy), with optoelectronic whirl flow meter. Spirometry was performed as stated by European Respiratory Society (14), using the European Community for Steel and Coal reference equations.

■ **Statistical analysis.** The Pearson correlation coefficient was used to correlate data. P values <0.05 were considered statistically significant.

RESULTS

All patients had perennial allergic rhinitis. All subjects were sensitised to house dust mite, 15 and 8 of them also to cat and dog allergen, respectively. On the basis of symptoms and FEV₁ measurements 44 subjects were classified as intermittent and 36 as mild persistent asthmatics, according to international guidelines (10).

Mean (+ SD) percentage of predicted FEV₁ was 80.8 ± 9.6. The mean of nasal eosinophil count was 7.6 ± 4.6. There was a significant correlation between nasal eosinophils and the percentage of predicted FEV₁ (figure 1, $r = -0.76$, $p < 0.001$).

DISCUSSION

Allergic rhinitis is sustained by an inflammatory response and eosinophil presence on nasal smear can be considered suggestive for an allergic reaction (6, 12). We previously reported a significant correlation between nasal symptoms and nasal eosinophils at baseline and after allergen challenge (15).

On the other hand, bronchial eosinophils are also present in asthma (16) and correlate with asthma severity (17).

Data comparing nasal and bronchial inflammation are progressively increasing. Chanaz *et al.* (18) demonstrated a higher number of eosinophils in bronchi than in nose in untreated asthmatics with perennial rhinitis, but in both cases eosinophils were activated. Crimi *et al.* reported no difference in bronchial eosinophil number in asthma and rhinitis, at baseline and after bronchial allergen challenge (19). Therefore, bronchial eosinophils are not unique and characteristic of asthma, and a clear link exists between upper and lower airways.

Our findings show an inverse relationship between eosinophil number and FEV₁ values, suggesting a possible role of nasal inflammation on bronchial airways, reinforcing the concept of "one airway-one disease" (3). To the best of our knowledge, this is the first study showing a significant correlation between nasal inflammation and lung function. Others have reported bronchial biopsy data from rhinitic subjects (19) or differences between upper and lower airway inflammation (18).

However, we are aware that a correlation between nasal inflammation and pulmonary function does not necessarily mean that nasal inflammation is responsible of bronchial asthma. It would be of great interest

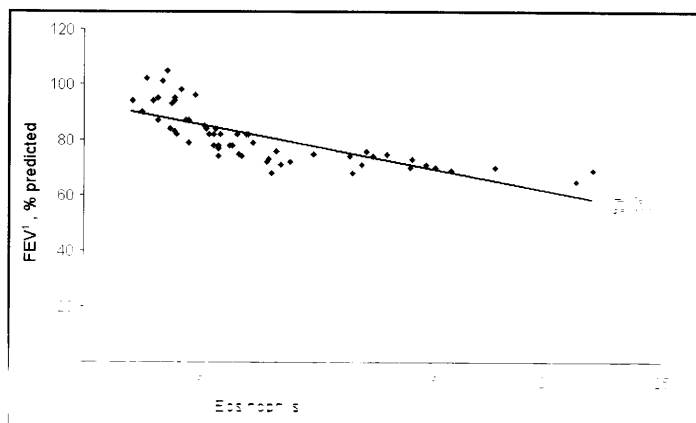


Figure 1: In perennial allergic rhinitis with concomitant asthma, there is a significant inverse relationship between percentage of predicted FEV1 and nasal eosinophil number ($r = -0.76$, $p < 0.0001$).

performing a similar study on asthmatic non-suffering from rhinitis, but extremely difficult due to the limited number of patients. Again, it would be of great interest treating these patients with nasal inhaled corticosteroids without treating concomitant asthma, but it appears ethically unacceptable. Nevertheless, our data strongly suggest that evaluating nasal inflammation may be an important non-invasive tool in routine examination of asthmatic subjects with concomitant referred rhinitis.

In conclusion, we have demonstrated a correlation between nasal inflammation and lung function, suggesting that nasal cytology might represent a common method to evaluate airway inflammation in asthmatic subjects with allergic rhinitis.

References

1. Simons FER. - Ancestors of Allergy. New York: Global Medical Communications, 1994.
2. Katelaris C.-H. - Allergic rhinitis and asthma: epidemiological evidence for the link. *Clin Exp All Rev* 2003;3:5-8.
3. Simons FER. - What's in a name? The allergic rhinitis-asthma connection. *Clin Exp All Rev* 2003;3:9-17.
4. Ciprandi G., Vizzaccaro A., Cirillo I. et al. - Increase of asthma and allergic rhinitis in Italian young men. *Int Arch Allergy Immunol* 1996;111:278-283.
5. Paulsen D.-F. - *Respiratory system*. In: Paulsen DF, ed. Basic Histology, 2nd edn. Englewood Cliffs: Prentice Hall, 1993;246-54.
6. Christodoulou P., Cameron L., Durham S., Hamid Q. - Molecular pathology of allergic disease. II Upper airway disease. *J Allergy Clin Immunol* 2000;105:211-23.
7. Foresi A., Leone C., Pelucchi A. et al. - Eosinophils, mast cells, and basophils in induced sputum from patients with seasonal allergic rhinitis and perennial asthma: relationship to methacholine responsiveness. *J Allergy Clin Immunol* 1997;100:58-64.
8. Hamid Q.-A., Minshall E.-M. - Molecular pathology of allergic disease. I Lower airway disease. *J Allergy Clin Immunol* 2000;105:20-36.
9. Bousquet J. - Requirements for medications commonly used in the treatment of allergic rhinitis. *Allergy* 2003;58:192-7.
10. Global Initiative for Asthma. - Pocket Guide for Asthma Management and Prevention. National Heart, Lung and Blood Institute, National Institute of Health, Bethesda, MD, 1997, NIH Publication no. 96-3659B.
11. Bousquet J., Van Cauwenberge P., Khaltaev N. - Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001;108(5 Suppl):S147-S334.
12. Ciprandi G., Tosca M.-A., Ricca V. et al. - Cetirizine treatment of rhinitis in children with pollen allergy: evidence of its antiallergic activity. *Clin Exp Allergy* 1997;27:1160-6.
13. Società Italiana di Allergologia e Immunologia Clinica - Memorandum della Diagnostica delle Allergopatie. *Fed Med* 1987;40:861-874.
14. Quanjer Ph.-H., Tammeling G.-J., Cotes J.-E., Pedersen O.-F., Peslin R., Yernault J.-C. - Standardized lung function testing. *Eur Respir J* 1993;6:1-99.
15. Ciprandi G., Pronzato C., Ricca V. et al. - Allergen-specific challenge induces ICAM-1 on nasal epithelial cells in allergic subjects. *Am J Resp Crit Care* 1994;150:1653-9.
16. Bousquet J., Chanez P., Lacoste J.-Y. et al. - Eosinophilic inflammation in asthma. *N Engl J Med* 1990;323:1033-9.
17. Kirby J.-C., Hargreave F.-E., Gleich G.-J., O'Byrne P.-M. - Bronchialveolar cell profiles of asthmatic and non-asthmatic subjects. *Am Rev Respir Dis* 1987;136:379-383.
18. Chanez P., Vignola A.-M., Vic P. et al. - Comparison between nasal and bronchial inflammation in asthmatic and control subjects. *Am J Respir Crit Care Med* 1999;159:588-95.
19. Crimi E., Milanese M., Oddera S. et al. - Inflammatory and mechanical factors of allergen-induced bronchoconstriction in mild asthma and rhinitis. *J Appl Physiol* 2001;91:1029-1034.

