Bronchial Hyperreactivity Is Related To Airflow Limitation And Independent Of Allergen Exposure In Hay Fever Patients

G Ciprandi, I Cirillo, A Vizzaccaro, C Klersy, G Marseglia, E Pallestrini

Citation

G Ciprandi, I Cirillo, A Vizzaccaro, C Klersy, G Marseglia, E Pallestrini. *Bronchial Hyperreactivity Is Related To Airflow Limitation And Independent Of Allergen Exposure In Hay Fever Patients*. The Internet Journal of Asthma, Allergy and Immunology. 2004 Volume 4 Number 1.

Abstract

Background: Bronchial hyperreactivity (BHR) and bronchial airflow limitation are frequently associated with allergic rhinitis.

Objective: the present study aimed at evaluating hay fever subjects to investigate the relationships among nasal TSS, nasal and bronchial airflow, and BHR both during and outside the pollen season.

Methods:Forty eight rhinitics sensitized to pollen allergens only were evaluated during and outside the pollen season. Rhinomanometry, spirometry, and methacholine bronchial challenge were performed.

Results: BHR was present in 26 patients during pollen season and in 27 outside pollen season. BHR was significantly related to nasal TSS, nasal airflow or FEF 25-75 values both during and outside pollen season. The relationship between BHR and FEF 25-75 was independent on allergen exposure.

Conclusion: This study provides evidence that nasal and bronchial airflow impairment are closely associated with BHR, whereas BHR is independent of allergen exposure in hay fever patients.

INTRODUCTION

in allergic rhinitis are caused by the IgE-dependent inflammatory cascade consequent to allergen exposure ($_{1}$). There is close association between allergen exposure and inflammatory events in allergic rhinitis as evidenced by the concept of minimal persistent inflammation ($_{2}$). In addition, allergen avoidance is typically characterized by the absence of both symptoms and nflammation as clearly demonstrated in hay fever patients outside the pollen season ($_{3}$).

Moreover, the ARIA document provided clear evidence concerning the link between upper and lower airways ($_{4}$). Allergic rhinitis and asthma frequently coexist as well; we reported that 77% of conscripts with respiratory allergy suffered from asthma associated with allergic rhinitis ($_{5}$). Allergic rhinitis has been demonstrated to be a strong risk factor for the onset of asthma, mainly when BHR is present ($_{6}$).

Very recently, we reported that hay fever patients frequently show early bronchial airflow impairment, as evidenced by low values of FEF 25-75, and BHR during the pollen season ($_{7}$).

Thus, this study aimed at evaluating a group of hay fever subjects perceiving nasal symptoms alone to investigate the relationships among nasal TSS, nasal and bronchial airflow, and BHR both during and outside the pollen season.

MATERIALS AND METHODS

STUDY DESIGN

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

Forty-eight hay fever patients were prospectively and consecutively evaluated (all males, age 22.8 ± 5.4 years). All of them were Navy soldiers who were referred to the Navy Hospital for periodic fitness visit. Subjects were visited during the spring 2003.All of them were evaluated with rhinomanometry, spirometry and methacholine bronchial challenge during the pollen(which pollen season, is there only one?) (in our region the most important allergenic pollens are grasses, Parietaria and Betulaceae that have the peak during the spring) season, i.e. in the spring. Successively, all of them were re-evaluated outside the pollen season, i.e. in the winter, a season without pollens in our geographic area ([3],[7]).

A detailed clinical history and a complete physical examination, including allergy evaluation, were performed. The patients were included in the study on the basis of a clinical history of seasonal(?Spring yes) allergic rhinitis and positive skin prick test only for pollens (including: Parietaria judaica, grasses(which Holcus lanatus, Cynodon dactylon and Lolium perenneolive tree, birch, and hazel(please provide scientific names for the trees/bushes) Betula alba Olea europaea, Corylus avellana) as described elsewhere ([3],[7]). None of the patients was a previous or a current smoker.

Skin prick test: Sensitization was assessed by performing skin prick test. It was performed as stated by the European Society of Allergy and Clinical Immunology ([8]). The allergen panel consisted of the following: house dust mites (Dermatophagoides farinae and pteronyssinus), cat, dog, grasses mix, Compositae mix, Parietaria judaica, birch, hazel tree, olive tree, Alternaria tenuis, Cladosporium, and Aspergilli mix; the concentration of allergen extracts was 100 I.R./mL (Stallergenes, Milan, Italy).

Nasal symptoms: The following symptoms were assessed by the patient, answering the questions made by the investigator, before and after treatment: nasal obstruction, sneezing, rhinorrhea, and itchy nose. Each symptom was evaluated on the following scale: 0= absent, 1= mild (symptom was present but was not annoying or troublesome), 2= moderate (symptom was frequently troublesome but did not interfere with either normal daily activity or sleep), and 3= severe (symptom was sufficiently troublesome to have interfered with normal daily activity or sleep). Total symptom score (TSS) being the sum of each individual symptom was also considered.

Rhinomanometry: Nasal airflow was measured by active anterior rhinomanometry. Patients wore a tight-fitting facemask, and with the mouth closed, breathed through one nostril. A sensor, placed in the contralateral nostril, recorded data on pre- and post-nasal pressures via airflow and pressure transducers. The instrument (ZAN 100 Rhino Flow Handy II, ZAN, Messgeraete Gmbh, Germany) was connected to a personal computer. The signals of transnasal airflow and pressure were amplified, digitized, and saved for statistical analysis.

Nasal airflow was reported as the sum of recorded airflow through right and left nostrils in milliliter per second at a pressure difference of 150 Pa across the nasal passage. Four or more airflow measurements were performed for each patient and the mean was recorded when reproducible values were achieved.

Spirometry: spirometry was performed with a computer-assisted spirometer (Pulmolab 435-spiro 235, Morgan, England) and according to the European Respiratory Society guidelines using the European Community for Steel and Coal reference equations ([9]).

Methacholine challenge: methacholine was administered using a dosimetric computerized apparatus (MEFAR MB3, Marcos, Italy), activated by the inhalator effort. Subjects inhaled progressively increasing doses of methacholine, starting from 30 µg until 1,200/ml µg in 11 steps. The procedure was stopped if and when the FEV1 fell by more than 20% from baseline. A computerized algorithm provided the provocation dose (PD_{20}) value. If no response was obtained with the maximal cumulative dose of 1,200 µg/ml, the test was considered negative.

Statistical analysis: This was performed with Stata 8, using Mann Whithey U test to compare the absolute value? Or percent predicted? If percent predicted used, please provide reference values/equation(see ref 9) used percent predicted values of FEF 25^{th}-75^{th} between positive and negative BHR patients and a general linear model to assess the association of log-transformed MCH and FEF 25-75, TSS or nasal air flow. Pearson R was computed.

RESULTS

All rhinitics were consecutive subjects meeting the inclusion and exclusion criteria and agreeing to join the study. No adverse event was reported during the study.

During pollen season findings: Twenty-six hay fever patients showed BHR. Patients with BHR showed significant lower values of FEF 25-75(absolute value or percent predicted?) percent predicted than rhinitics without BHR (median 84 vs 97, $p<0.001$) (Figure 1). In patients with BHR, significant correlations were present between MCH (log-transformed) and FEF 25-75 values (R=.74, p<0.001), nasal TSS (R=-.58, p=0.002) or nasal airflow (R=.56, p=0.003) (Figure 1 and 2).

Figure 1

Figure 1 : Upper left panel - Comparison of FEF 25-75 levels between patients with positive and negative MCH during pollen season Lower left panel - Association of MCH (log transformed) and TSS during pollen season (patients with positive MCH only) Lower right panel - Fig 1D: Association of MCH (log transformed) and nasal flow during pollen season (patients with positive MCH only) boxes represent the interquartile range, whiskers the non outliers extreme; outliers are shown as single dots.

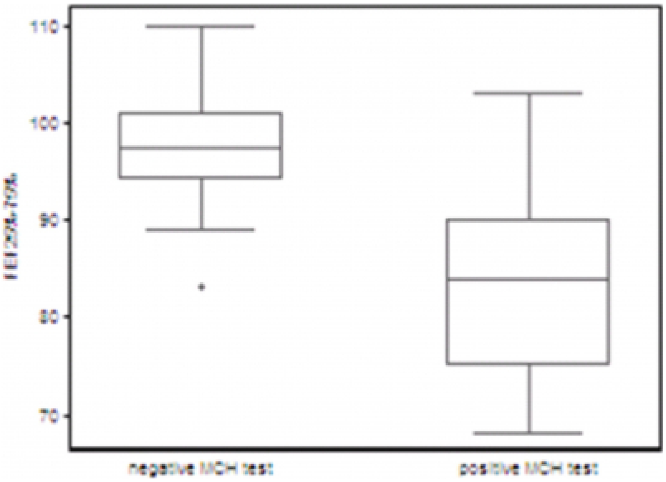


Figure 2

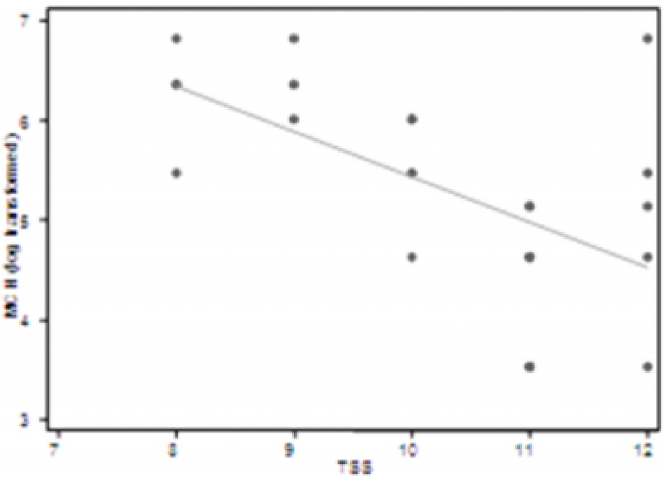


Figure 3

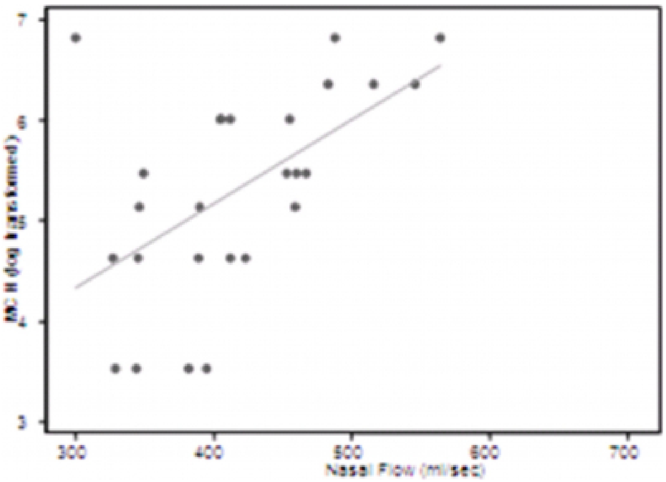


Figure 4

Figure 2: Association of MCH (log transformed) and FEF 25-75 during (left) and outside pollen season (right)

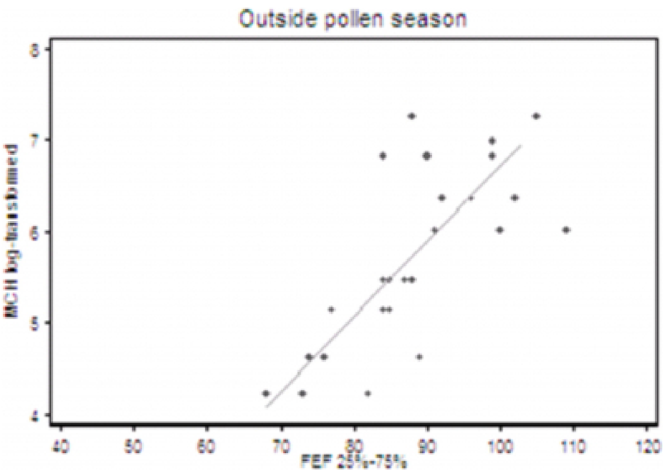
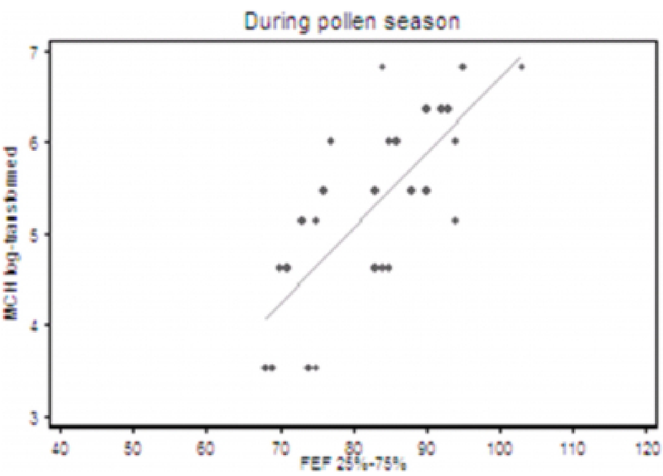


Figure 5



Outside pollen season findings: Twenty-seven hay fever patients showed BHR. Patients with BHR showed significant lower values of FEF 25-75 than rhinitics without BHR (median 88 vs 102, p=0.001)(again is this percent predicted? yes). In patients with BHR, significant correlations were present between MCH (log-transformed) and FEF 25-75 values (R=.75, p<0.001), nasal TSS (R=-. 69, p<0.001), or nasal airflow (R=.51, p=0.006).

With multivariate analysis, the association between MCH (log-transformed) and FEF 25-75 in patients with BHR proved both independent from season (p<0.001) and of a similar magnitude in both periods (p for interaction=0.603) (figure 2).

DISCUSSION

The present findings suggest some considerations concerning the link between upper and lower airways and the variations of respiratory parameters consequent on allergen exposure in patients with hay fever.

Firstly, BHR is detectable in more than 50% of patients and its prevalence is substantially independent of allergen exposure. BHR positive subjects showed lower FEF 25-75 values than BHR negative patients and this finding persists also outside the pollen season. There is moreover a significant relationship between FEF 25-75 values and BHR. FEF 25-75 has been proposed as a marker of small airways impairment ([10]) and we very recently demonstrated that reduced FEF 25-75 values and BHR were common findings in hay fever patients ([7]). It is noteworthy to underline that the relationship between FEF 25-75 and BHR is present also outside the pollen season. These results support the concept that BHR in hay fever constitutes a pathophysiologic event appearing to be independent of allergen exposure. Thus, whereas allergen exposure is the necessary event capable of inducing the occurrence of inflammation and symptoms, BHR appears to be a constant and independent variable.

Secondly, nasal symptom intensity and nasal airflow limitation are closely associated with BHR. This issue highlights the importance of upper airways in inducing and worsening BHR. It is of note that these relationships persist also outside the pollen season, probably as consequence of hypertrophic turbinates.

In conclusion, this study provides evidence that nasal symptoms and nasal airflow impairment as well as early bronchial airflow limitation are closely associated with BHR, whereas BHR is independent of allergen exposure in hay fever patients.

CORRESPONDENCE TO

Giorgio Ciprandi, M.D. Allergologia - U.O. ORL Dipartimento Regionale Testa-Collo Padiglione Specialità (piano terzo) Ospedale San Martino Largo R. Benzi 10, 16132 Genoa, Italy Phone 00 39 10 5552124 FAX 00 39 10 5556682 E-mail gio.cip@libero.it

References

1. Van Cauwenberger P, De Belder T, Vermeiren J, Kaplan A Global resources in allergy (GLORIA): allergic rhinitis and conjunctivitis. Clin Exp All Rev 2003;3:46-50
2. Ciprandi G., Buscaglia S., Pesce G.P., Pronzato C., Ricca V., Parmiani S., et al. "Minimal persistent inflammation is present at mucosal level in asymptomatic rhinitic patients with allergy due to mites. J. Allergy Clin. Immunol. 1995;96:971-979
3. Ciprandi G., Pronzato C., Ricca V., Bagnasco M., Canonica G.W. "Evidence of intercellular adhesion molecule-1 expression on nasal epithelial cells in acute rhinoconjunctivitis caused by pollen exposure". J. Allergy Clin. Immunol. 1994;94:738-746
4. Bousquet J, Van Cauwenberg P. Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol 2001;108:S1-315
5. Ciprandi G, Vizzaccaro A, Cirillo I et al. Increase of asthma and allergic rhinitis prevalence in young Italian men. Int Arch Allergy Immunol 1996;111:279-83
6. Braman SS, Barrows AA, DeCotiis BA, et al. Airway hyperresponsiveness in allergic rhinitis : a risk factor for asthma. Chest 1987 ;91 :671-4.
7. Ciprandi G, Cirillo I, Tosca MA, Vizzaccaro A. Bronchial hyperreactivity and spirometric impairment in patients with seasonal allergic rhinitis. Resp Med 2004;98:826-31
8. Dreborg S (Ed.). EAACI Subcommittee on Skin Tests. Skin tests used in type I allergy testing. Position Paper. Allergy 1989; 44 (Suppl.10):22-31
9. Quanjer PH, Tammeling GJ, Cotes JE, et al. Standardized lung function testing. Eur Respir J 1993;6:1-99
10. Stahl E Correlation between objective measures of airway calibre and clinical symptoms in asthma: a systematic review of clinical studies. Resp Med 2000;94:735-41

Author Information

Giorgio Ciprandi, M.D.
Ospedale San Martino

Ignazio Cirillo, M.D.
Ospedale Marina Militare

Andrea Vizzaccaro, M.D.
Ospedale Marina Militare

Catherine Klersy, M.D.
Servizio di Biometria ed Epidemiologia Clinica, Direzione Scientifica, IRCCS Policlinico

Gian Luigi Marseglia, M.D.
Clinica Pediatrica, IRCCS Policlinico

Eugenio Pallestrini, M.D.
Ospedale San Martino