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Bronchial hyperreactivity and spirometric impairment in polysensitized patients with allergic rhinitis

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Abstract

Background: We previously demonstrated in a group of patients with perennial allergic rhinitis alone impairment of spirometric parameters and high percentage of subjects with bronchial hyperreactivity (BHR). The present study aimed at evaluating a group of polysensitized subjects suffering from allergic rhinitis alone to investigate the presence of spirometric impairment and BHR during the pollen season.

Methods: One hundred rhinitics sensitized both to pollen and perennial allergens were evaluated during the pollen season. Spirometry and methacholine bronchial challenge were performed.

Results: Six rhinitics showed impaired values of FEV1 without referred symptoms of asthma. FEF 25–75 values were impaired in 28 rhinitics. Sixty-six patients showed positive methacholine bronchial challenge. FEF 25–75 values were impaired only in BHR positive patients ($p < 0.001$). A significant difference was observed both for FEV1 ($p < 0.05$) and FEF 25–75 ($p < 0.001$) considering BHR severity.

Conclusions: This study evidences that an impairment of spirometric parameters may be observed in polysensitized patients with allergic rhinitis alone during the pollen season. A high percentage of these patients had BHR. A close relationship between upper and lower airways is confirmed.

Background

Close association between allergic rhinitis and asthma has been demonstrated by several studies [1-3]. Moreover, allergic rhinitis has been demonstrated to be a strong risk factor for the onset of asthma in adults [4].

Asthma is characterized by a reversible airflow obstruction and forced expiratory volume/1 second (FEV1) is considered the main parameter to evaluate bronchial obstruction [5]. Nevertheless, there is increasing interest to consider the involvement of small airways in the pathogenesis of asthma [6]. Even though there is no direct parameter cap able of assessing small airways, it has been assumed that the forced expiratory flow at the 25 and 75% of the pulmonary volume (FEF 25–75) might be considered as a measure of the caliber concerning distal airways

[7]. Particularly, subjects with mild asthma and normal FEV1 may show impaired FEF 25–75 only [8]. On the other hand, bronchial hyperreactivity (BHR) is a paramount feature of asthma. Moreover, BHR may be observed in a proportion of rhinitics [9]. In this regard, it has been hypothesized that a positive bronchial challenge to methacholine could be considered as predictive for those rhinitics would progress to develop asthma [10]. In addition, a seasonal variability in BHR was described in subjects sensitized to pollens [11]. Very recently, we demonstrated that patients with perennial allergic rhinitis alone frequently showed impaired spirometric parameters and positive methacholine challenge [12].

On the basis of these considerations, we aimed at evaluating a group of polysensitized patients with allergic rhinitis alone to investigate the presence of spirometric abnormalities and BHR during the pollen season.

Materials and methods

Study design

The study was performed during the pollen season (when patients were symptomatic), from April to May. To evaluate spirometric abnormalities and the presence of BHR in patients with pure rhinitis, we included subjects with allergic rhinitis due both to pollen and perennial allergens. We excluded all the subjects who met the following exclusion criteria: asthma symptoms, including cough, wheezing, dyspnoea, chest tightness, and shortness of breathing, acute upper respiratory infections and use of nasal or oral corticosteroids, and antihistamines within the previous 4 weeks.

The study was approved by the Institutional Review Board of Navy Hospital, an informed consent was obtained from patients, and was in compliance with the Helsinki Declaration.

Subjects

One hundred rhinitic patients were prospectively and consecutively evaluated, all males, age 23.4 ± 3.8 years. All of them were Navy soldiers who referred to Navy Hospital for periodic fitness visit. All of them were evaluated performing both spirometry and methacholine bronchial challenge during the pollen season, i.e. in the spring, season with pollens in our geographic area [3].

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 allergic rhinitis. All patients were sensitized both to pollens (i.e. *Parietaria officinalis*, grasses, olive tree, birch, or hazel) and perennial allergens (i.e. house dust mites, cat, or dog). The diagnosis of allergic rhinitis was made on the basis of a history of nasal symptoms and positive skin prick test as described elsewhere [3]. None of the patients was a previous or a current smoker.

Skin prick test

it was performed as stated by the Italian Society of Allergy and Clinical Immunology [13]. The panel consisted of: house dust mites (*Dermatophagoides farinae* and *pteronyssinus*), cat, dog, grasses mix, *Compositae* mix, *Parietaria officinalis*, birch, hazel, olive tree, *Alternaria Tenuis*, *Cladosporium*, *Aspergilli* mix (Stallergenes, Milan, Italy).

Spirometry

It was performed by using a computer-assisted spirometer (Pulmolab 435-Spiro 235, Morgan, England), with optoelectronic whirl flow meter. Spirometry is performed as stated by European respiratory Society [14], using the European Community for Steel and Coal reference equations.

If an airway obstruction was present as detected by FEV1 values less than 80% of the predicted, a test of bronchodilatation was performed using a salbutamol metered dose of 200 mcg. Reversibility was considered if an increase of at least 12% of FEV1 from baseline was achieved, according to international guidelines [15].

Methacholine bronchial challenge

It was performed to evaluate BHR only if basal FEV1 was equal or more than 80% of predicted. Aerosol is delivered using a dosimetric computerized supply (MEFAR MB3, Marcos, Italy). Subjects inhaled increasing doses of methacholine, starting from 34 μg/mL. The scheduled doses consisted of the following: 34, 68, 68, 68, 170, 170, 340, 170, 340, 170 μg/mL as previously reported [3,12].

The test was interrupted when FEV1 value was reduced by more or equal than 20% of control or a maximal cumulative dose of 1,598 μg/ml was achieved. The threshold dose causing a 20% fall of FEV1 (PD20) was calculated.

Degree of BHR

Four arbitrary classes of BHR were considered: very mild = PD20 > 400 μg/mL, mild = PD20 ranging from 201 to 400 μg/mL, moderate = PD20 ranging from 200 to 101 μg/mL, and severe = PD20 < 100 μg/mL as previously reported [6,16].

Statistical analysis

Statistical analysis was performed using X square test, calculating confidential limits of the relative risk at 95%. Differences were considered significant if p values were <0.05. Data are presented as means.

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.

Sensitizations

all subjects were sensitized both to perennial allergens and pollen allergens. Twenty subjects had 2 sensitizations, 34 had 3 sensitizations, and 46 had more than 3 sensitizations. There was no relationship between number of sensitizations and spirometric data.

Spirometry

six patients showed a FEV1 value less than 80% of the predicted. It has to be mentioned that all of them were completely asymptomatic for complaints concerning lower airways. A bronchial reversibility was achieved in all subjects.

In addition, 7 patients showed impaired FVC values and 28 patients showed abnormal FEF 25–75 values.

Methacholine bronchial challenge

it was performed in 94 rhinitics. Sixty-six rhinitics showed a positive methacholine challenge. On the basis of BHR degree, we subdivided the methacholine positive patients in 4 groups: very mild, mild, moderate, and severe. Seventeen patients had a very mild degree of BHR, 16 had a mild degree, 10 had a moderate degree, and 23 a severe degree.

Then, we analyzed subjects subdividing them in two groups: patients with BHR (BHR positive group) and patients without BHR (BHR negative group). Thus, we evaluated the distribution of the patients considering FEV1, FVC, and FEF 25–75 values (Figure 1). FEV1 values were normal in both groups. Five subjects in the BHR positive group and 2 in the BHR negative group had reduced values of FVC only. FEF 25–75 values were reduced in 28 subjects of BHR positive group only ($p < 0.001$).

We considered the three spirometric parameters related with BHR degree (Figure 2). A significant difference was observed for both FEV1 and FEF 25–75 considering BHR severity in subjects with moderate BHR ($p < 0.001$ for FEF 25–75 only) and with severe BHR ($p < 0.05$ for FEV1 and $p < 0.001$ for FEF 25–75).

Discussion

Allergic rhinitis and asthma should be considered as a single syndrome involving two parts of the respiratory tract, even though it is evident that these two disorders affect each other [16].

Allergic rhinitics frequently present a non-specific BHR even in absence of asthmatic symptoms. In these subjects with normal FEV1 values, BHR may be envisaged as a marker of susceptibility to develop asthma. On the other hand, in mild asthmatics during intercritical periods lung function may be normal concerning FEV1 values [17]. Moreover, asthma is a chronic inflammatory disease of airways and using other parameters it has been demonstrated a persistence of inflammation, also in absence of symptoms, mainly involving smaller airways [18]. In these cases, abnormal FEF 25–75 values may be observed: it has been reported that FEF 25–75 may be reduced in asthmatics with normal FEV1 and FVC values [8]. It has been suggested that FEF 25–75 might be considered a marker of small airways impairment in mild asthmatics with normal FVC values [7].

Very recently, we demonstrated some interesting findings in a group of 100 patients with perennial allergic rhinitis alone [12]. Five patients showed impaired FEV1 values (<80% of predicted), without any perceived lower respiratory symptoms [12]. Moreover, 72 patients showed positive methacholine challenge, and there was a significant relationship between BHR degree and FEV1 and FEF 25–75 values [12]. Thus, we aimed at investigating a large group of polysensitized patients with allergic rhinitis during the pollen season to evaluate spirometry and BHR.

The present findings suggest some considerations concerning the link between upper and lower airways.

Firstly, evaluating a large cohort of polysensitized subjects with allergic rhinitis alone, it is possible to single out some subjects (six) with overt bronchial obstruction, as documented by impaired FEV1 values. These patients may be considered as "poor perceiver" of their lower respiratory symptoms. In fact, all of them had a normal life playing different sports without trouble. In addition, they never felt lower respiratory symptoms nor diagnosis of asthma has been made. It is noteworthy that this finding confirms that demonstrated in perennial rhinitics (5 patients with overt bronchial obstruction).

Secondly, most of our rhinitics (66 subjects) showed BHR. This finding is not surprising if compared with literature analysis and confirm our previous findings in patients with perennial allergic rhinitis. The exposure to allergens is characterized by nasal inflammation as previously described by ourselves [19]. This concept may be consistent with a consequent bronchial inflammation. It is noteworthy that BHR was asymptomatic in all our rhinitics.

Thirdly, considering the evaluation of FEF 25–75 parameter we demonstrated that some rhinitics (28 subjects)

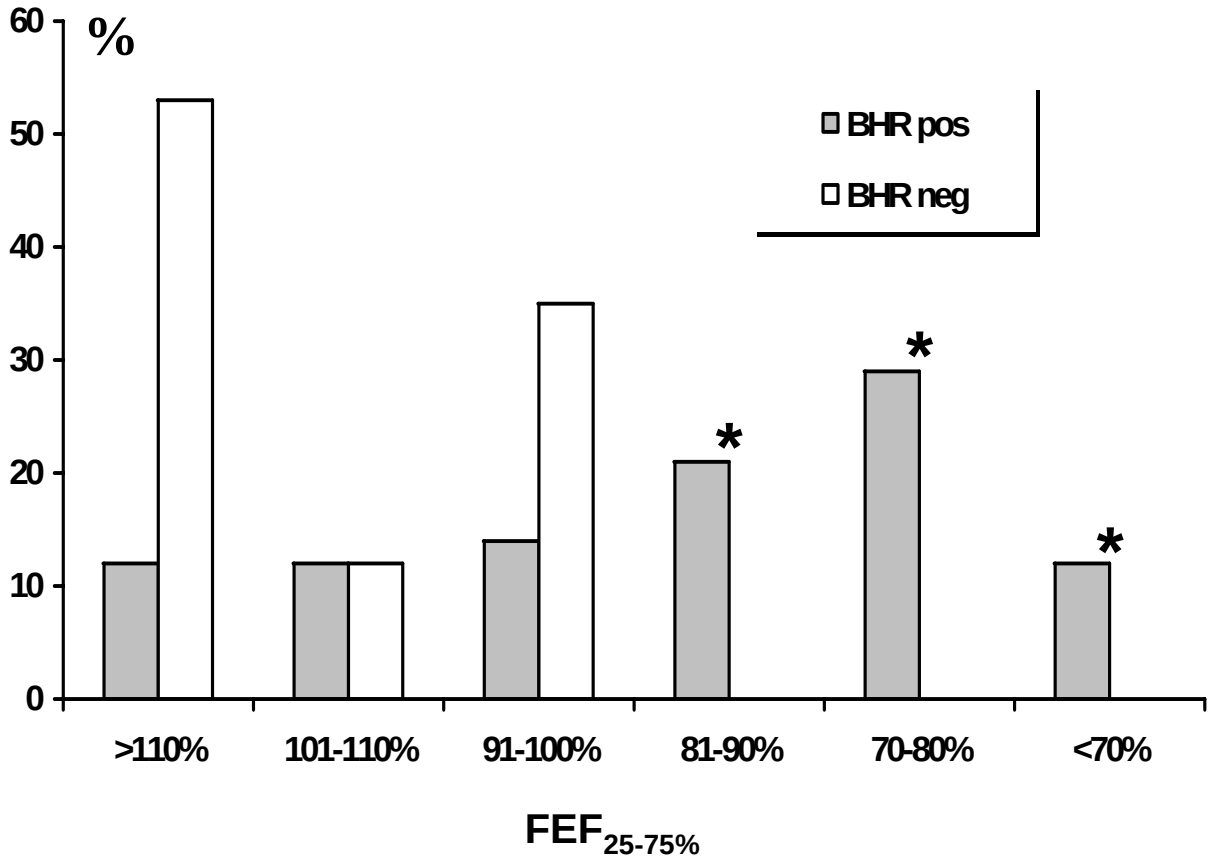

Figure 1
Percentage distribution of FEF 25–75 values (as % of predicted) in BHR positive and BHR negative patients.

shows an initial level of bronchial obstruction during the pollen season. It has to be highlighted that BHR positive patients only showed this impairment. This finding may underline the relevance of considering this parameter as it was impaired only in BHR subjects. Thus, FEF 25–75 could be envisaged as marker of bronchial involvement in pure rhinitics with BHR.

Fourthly, there is a relationship between degree of BHR and FEV1 and FEF 25–75 impairment. These last findings underline the relationship between BHR and airway caliber in patients with airway inflammation. Moreover, these data, taken together, partially confirm previous results observed in patients with perennial allergic rhinitis alone [12]. Polysensitized patients with allergic rhinitis, compared with patients with perennial allergic rhinitis, even more show an association with asthma, the impairment of FEF 25–75, the BHR, and the relationship between BHR grade and spirometric abnormalities. Actually, it is clear that allergic inflammation is chronic in these subjects and it is exacerbated by pollen exposure.

Conclusions

The present study highlights the frequent coexistence of bronchial impairment in polysensitized patients with allergic rhinitis alone during the pollen season and supports the strong link between upper and lower airways. Thus, a careful evaluation of lower airways should be performed also in those patients with allergic rhinitis alone.

List of abbreviations

BHR: bronchial hyperreactivity

FEV1: forced expiratory volume in 1 second

FEF: forced expiratory flow

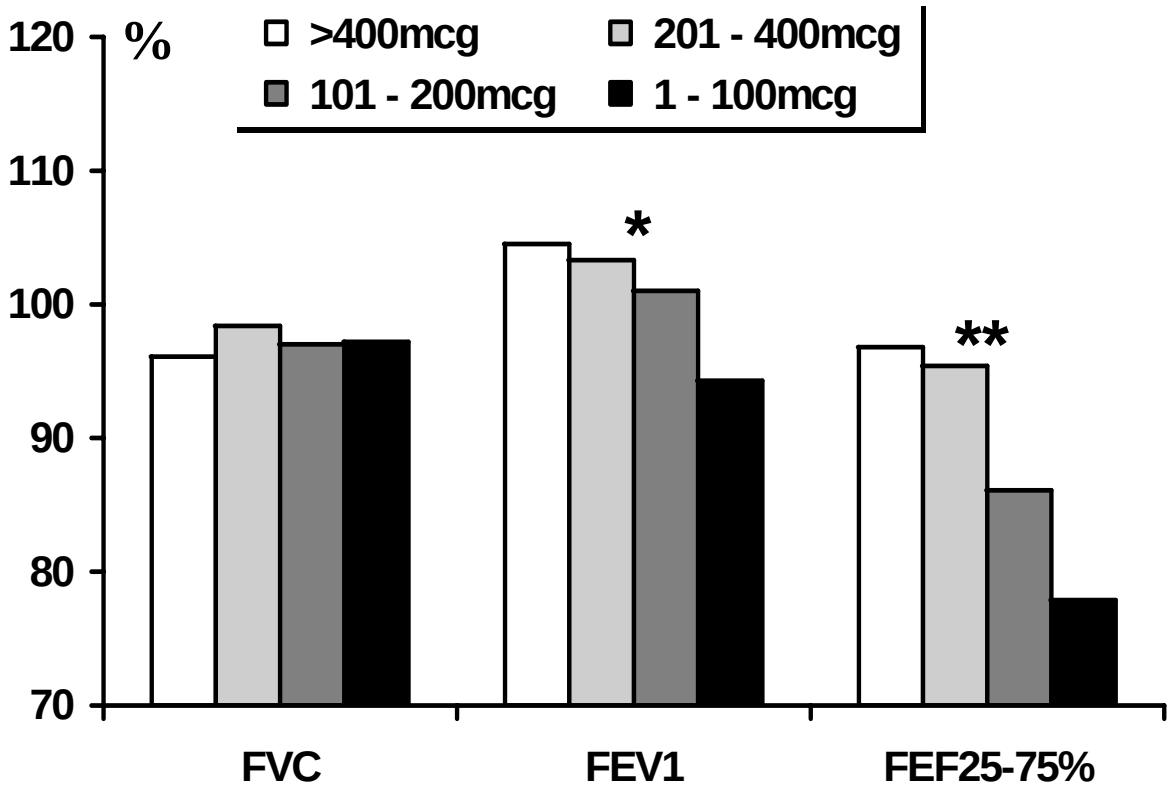

Figure 2
Percentage distribution of mean values of FVC, FEV1, and FEF 25–75 in comparison with BHR grade.

FVC: forced volume capacity

Competing interests
None declared.

Authors' contributions
GC conceived of the study, and participated in its design and coordination, IC participated in the design of the study and performed the statistical analysis, MAT revised the manuscript, and AV participated in the clinical study. All authors read and approved the final manuscript.

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