

SCREENING SPIROMETRY TO DETECT RESPIRATORY ALLERGY

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SUMMARY:

■ **Background:** Recently, it has been evidenced that the forced expiratory flow at the 25 and 75% of the pulmonary volume (FEF₂₅₋₇₅) might be considered as a possible marker of early bronchial impairment in patients with allergic rhinitis alone.

■ **Objectives:** The aim of this study was to determine whether a spirometric impairment may predict allergy during screening visit.

■ **Methods:** The study included 283 Navy soldiers (255 males, mean age 27.1 + 8.2) who had to undergo spirometry for attending specific courses. Fifty-four showed slight spirometric anomalies. Thus, they referred to Navy Hospital of La Spezia for standardized tests: skin prick test, spirometry, and methacholine bronchial challenge.

■ **Results:** Forty seven (87%) subjects were sensitized (47% monosensitized and 53% polysensitized). Allergic rhinitis was diagnosed in 25 subjects with median nasal TSS 5. FVC and FEV1 values were normal, whereas FEF₂₅₋₇₅ values were reduced (61.8 + 14.8 % of predicted), bronchodilation test was significant for FEF₂₅₋₇₅ (82.9 + 16.8% of predicted; $p < 0.001$) only. Bronchial hyperreactivity (BHR) was detected in 28 subjects, all but 1 were sensitized.

■ **Conclusions:** This study provides evidence, relevant to clinical care, that mild spirometric impairment may generate the suspect of allergic disorders, thus spirometry could be more frequently performed in general population screening.

Key-words: Sensitization - Rhinitis - Spirometry - FEF₂₅₋₇₅, bronchial hyperreactivity

INTRODUCTION

Close association between allergic rhinitis and asthma has been reported (1). Moreover, allergic rhinitis has been demonstrated to be a strong risk factor for the onset of asthma in adults (2).

Asthma is characterized by a reversible airflow obstruction and inflammation of airways is involved in the pathogenesis of asthma (3). The forced expiratory flow at the 25 and 75% of the pulmonary volume (FEF₂₅₋₇₅) might be considered as a possible marker of early bronchial impairment in patients with allergic rhinitis alone (4, 5, 6). On the other hand, bronchial hyperreactivity (BHR) is a paramount feature of asthma and may be observed in a high proportion of rhinitics, sensitized to perennial allergens (5), pollens (6), or both (4). In addition, Th2-dependent cytokines and eosinophilic inflammation are related with nasal and bronchial airflow impairment in rhinitics (7, 8).

Therefore, the aim of this study was to determine whether a spirometric impairment in a cohort of

young subjects, likely healthy as being Navy soldiers, may predict allergy during screening visit.

MATERIALS AND METHODS

■ **Study design:** The study included a cohort of Navy soldiers. All of them were, of course, healthy subjects, continuously trained and checked. All of them had to carry out specialistic examinations, including spirometry, to obtain the fitness for attending specific courses (e.g. for frogman, diver, submariner, etc.).

The Review Board approved the study and an informed consent was obtained from each subject.

■ **Subjects:** In the first part, spirometry was performed in 283 Navy soldiers (255 males, mean age 27.1 + 8.2). Further, fifty-four showed slight spirometric anomalies concerning the flow-volume curve, including hysteresis (41 subjects) and Peak Expiratory Flow (13 subjects). Thus, they referred to Navy Hospital of La Spezia for standardized assessments.

Detailed clinical history, complete physical examination, skin prick test, spirometry, and methacholine bronchial challenge were performed in all subjects.

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The diagnosis of allergic rhinitis was made on the basis of history of nasal symptoms and positive skin prick test according with validated criteria (1).

It is noteworthy of mentioning that all of them were completely symptomless for complaints concerning lower airways, as that is incompatible with military service.

Nobody had assumed nasal or oral corticosteroids, and antihistamines within the previous 4 weeks.

■ **Skin prick test:** Allergy was assessed by the presence of sensitization to the most common classes of aeroallergens by performing skin prick test. It was performed as stated by the European Academy of Allergy and Clinical Immunology (9). 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). A histamine solution in distilled water (10 mg/mL) was used as positive control and the glycerol-buffer diluent of the allergen preparations as negative control. Each patient was skin tested on the volar surface of the forearm using 1 mm prick lancets (Stallergenes, Milan, Italy). The skin reaction was recorded after 15 minutes by evaluating the skin response rate to the inoculation of each allergen extract in comparison with the wheal given by the positive and the negative control. A wheal diameter equal or greater than 3 mm was considered a positive reaction.

■ **Nasal symptoms:** The following symptoms were assessed by the subject, answering the questions made by the investigator: 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 considered.

■ **Spirometry:** It was performed by using a computer-assisted spirometer (Pulmolab 435-spiro 235, Morgan, England), with optoelectronic whirl flow meter. Spirometry was performed as stated by European Respiratory Society (10). If an airway obstruction was present as detected by FEV1 values less than 80% of the predicted, a test of bronchodilation 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 (11). About FEF₂₅₋₇₅, reversibility was considered when there was an increase of at least 15% from baseline values (12).

■ **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 30 mcg/mL. The scheduled doses consisted of the following: 30, 30, 30, 60, 90, 150, 150, 300, 300, 300, 150 mcg/mL as previously reported (4, 5, 6).

The test was interrupted and considered positive when FEV1 value was reduced by more or equal than 20% of control or a maximal cumulative dose of 1,590 mcg/ml was achieved. The threshold dose causing a 20% fall of FEV1 (PD20) was calculated.

■ **Statistical analysis:** Paired comparisons of lung function parameters were performed with the paired t test. The association of patients' characteristics with the change in FEF₂₅₋₇₅ was assessed by means of a general linear regression model. For post-hoc comparisons, significance was set at 0.017 (Bonferroni correction for 3 comparisons). Stata 8 (College Station, TX) was used for computation.

RESULTS

Forty seven (87%) subjects were sensitized (47% monosensitized and 53% polysensitized). Allergic rhinitis was diagnosed in 25 subjects with median nasal TSS 5. FVC and FEV1 values were normal, whereas FEF₂₅₋₇₅ values were reduced (61.8 + 14.8 % of predicted), bronchodilation test was significant for FEF₂₅₋₇₅ (82.9 + 16.8%; $p < 0.001$) only. Bronchial hyperreactivity (BHR) was detected in 28 subjects, all but 1 were sensitized.

The possible clinical correlates of the change in FEF were investigated by means of a regression model. Significantly higher reversibility was shown in males ($p < 0.01$); in patients with single or multiple sensitivities ($p < 0.01$), with higher nasal TSS ($p < 0.05$), and with BHR ($p < 0.01$) (Figure 1).

DISCUSSION

Evaluating substantially healthy subjects, such as military personnel well trained and checked, spirometry

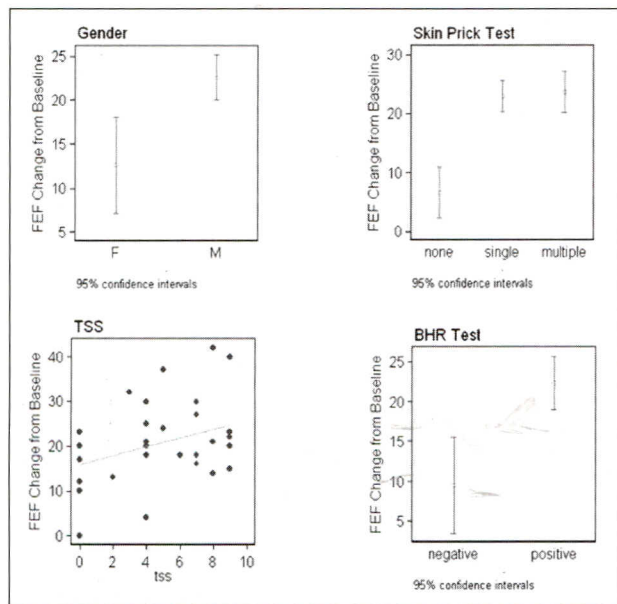


Figure 1: Clinical correlates of change in FEF₂₅₋₇₅. Mean and 95%CI are presented for categorical variables, scatter plot and linear regression line for continuous variables.

testing may reveal a slight impairment that may justify more appropriate assessments useful to detect allergic disorders. In fact, nasal symptoms, sensitizations, and BHR, appeared to be strongly associated with a reduced FEF₂₅₋₇₅. Moreover, the FEF₂₅₋₇₅ reversibility was related with increasing severity of nasal symptoms and BHR. Our findings furthermore support the concept of a link between allergic inflammation and increased bronchial reactivity in sensitized subjects.

Moreover, it is noteworthy that the lowest FEF₂₅₋₇₅ values were shown in those subjects with nasal symptoms, and severe BHR. Thus, FEF₂₅₋₇₅ values may be envisaged as possible marker of early bronchial involvement in atopic subjects as previously reported (5, 6). On the other hand, FEF₂₅₋₇₅ reversibility is actually associated with polysensitization, severity of nasal symptoms, and degree of BHR. Thus, also this issue deserves consideration as it underlines that reversibility of FEF₂₅₋₇₅ may mean reliable marker of early bronchial airflow impairment in atopic subjects.

In conclusion, this study provides evidence, relevant to clinical care, that mild spirometric impairment may generate the suspect of allergic disorders, thus spirometry could be more frequently performed in general population screening.

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