Pulmonary function tests and impulse oscillometry in severe chronic obstructive pulmonary disease patients’ offspring

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Background: Several studies have showed an increased prevalence of airflow obstruction in first degree relatives of individuals with chronic obstructive pulmonary disease (COPD). Considering no specific research had evaluated airway resistance in offspring of patients with severe COPD, we utilized a spirometry and a impulse oscillometry (IO) to evaluate this population. Materials and Methods: In this case control study, from November 2011 to July 2012, we consecutively evaluated 54 offsprings of severe COPD patients (case group) admitted in the pulmonary ward, affiliated to the Isfahan University of Medical Sciences and control group. Pulmonary function tests and the IO were obtained for both groups. Student’s t-test was used for inter-group comparisons, and P values below 0.05 were taken as significant. Results: Abnormal increased airway resistance was seen in cases in comparison with controls (R5 Hz [46.29%, P = 0.01], R25 Hz [42.59%, P < 0.001]). Also, considering the spirometry, case group had pulmonary function parameters less than control group (forced vital capacity [FVC]; P = 0.02, forced expiratory volume in 1st s; P < 0.001, forced expiratory flow (FEF) 25-75; P < 0.001, FEF 25-75/FVC; P < 0.001) but they were in normal range. Conclusion: This study demonstrated increased airway resistance among the severe COPD offsprings. The IO may be a sensitive tool for detection of high risk subjects in families with COPD.

Key words: Chronic obstructive pulmonary disease, impulse oscillometry, offspring, pulmonary function tests

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a lung disease characterized by chronic obstruction of lung airflow that interferes with normal breathing and is not fully reversible. COPD is a leading cause of morbidity and mortality worldwide and results in economic and social burden that is both substantial and increasing.

Several studies subsequently reported significant familial correlation of forced expiratory volume in 1st s (FEV1) in different populations (range 0.11-0.66) in nuclear families. These cross-sectional studies suggest a strong genetic component relating susceptibility to smoking and rate of decline in FEV1. The family history of COPD is a strong risk factor for COPD, independent of family history of smoking, personal lifetime smoking, or childhood environmental tobacco smoke exposure. Genetic contributions to pulmonary function have been supported by both studies in the general population and twin studies. To date, alpha-1-antitrypsin deficiency is the only proven genetic risk factor for COPD; however, this genetic disorder is very rare in Asian countries and it is not an important risk factor for the development of COPD in Asian population. Familial aggregation of and genetic contributions to COPD, a disease characterized by obstructive abnormalities in pulmonary function, have been extensively investigated. Several early studies showed an increased prevalence of airflow obstruction in first degree relatives of individuals with COPD compared with control subjects. Identifying...
intermediate phenotypes other than FEV₁ and FEV₁/FVC forced vital capacity (FVC) for genetic linkage and association studies of COPD may provide further understanding of risk factors for lung function decline and genetic influences on obstructive pulmonary disease.\cite{10} Airway wall thickening and emphysema show independent familial aggregation in COPD.\cite{11}

Several studies have showed an increased prevalence of airflow obstruction in first degree relatives of individuals with COPD. Considering no specific research had evaluated airway resistance in offspring of patients with severe COPD, we utilized the spirometry and the impulse oscillometry (IO) to evaluate pulmonary function tests and the IO in severe COPD patients’ offspring.

MATERIALS AND METHODS

The Ethics Committee of the Isfahan University of Medical Sciences approved the research protocol (research project number: 385485). All participants or their guardians provided written consent for research.

In this case control study, from November 2011 to July 2012, we consecutively evaluated 54 offsprings of severe COPD patients (a diagnosis was made on the basis of the clinical history, physical examination, and pulmonary function tests, performed within the last 12 months and staging was based on GOLD\cite{12}) admitted with COPD exacerbation in pulmonary ward at the Noor Hospital (Isfahan, Iran). During the observation period, 20 COPD patients were identified from medical records in the hospital. All of 82 available offspring of these patients were invited to enroll in this research. However, 54 offsprings of the COPD patients participated in this research. Offsprings with chest wall deformity, pregnancy, smoking, high risk jobs for the respiratory system, recent respiratory infection, pulmonary and cardiac diseases did not include. We defined an abnormal pulmonary function as FEV₁ and FVC <80% of predicted values and FEV₁/FVC <0.7.\cite{13} We also defined abnormal airway resistance higher than mean values of control subjects plus 2 times of standard deviation in the IO.\cite{14}

People who were matched in effective factors on pulmonary function including age, sex, and height were randomly selected from our previous population-based study. The detailed design and operation of this study were described previously.\cite{14}

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FVC and FEV₁, forced expiratory flow 25-75 (FEF), and FEF 25-75/FVC was measured by standard the spirometry. The detailed protocol of lung function measurements and instruments used in this study were previously described.\cite{15} This was followed by the IO, using a standard technique for measurement of airway resistance, reactance, and impedance.\cite{16}

The data are reported as mean (median, interquartile range). Student’s t-test was used for inter-group comparisons, and P values below 0.05 were taken as significant. The SPSS for windows (Version 16.0, 2007, SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

RESULTS

The cases and controls had similar age, height, and sex distribution. The demographic characteristics of the two populations are reported in Table 1. Mean resistance (R) was significantly greater in the case group than the control group both at 5 Hz and at 25 Hz. Reactance (X) was similar in the case group and the control group at 5 Hz but was lower in the cases at 25 Hz [Table 2].

The quantitative data related to abnormal pulmonary function and increased airway resistances are shown in Table 3. The definition of increased airway resistance is based on our previous study.\cite{13}

DISCUSSION

Our results demonstrate conclusively the familial clustering of airflow obstruction in COPD offspring (cases). Our study

| Table 1: Demographic characteristics of case and control group |
|-----------------|-----------------|-----------------|
| Parameters      | Case (n = 54)   | Control (n = 54) |
| Age (year)      | 34.26 (21, 34.50)| 34.22 (21, 34.50) |
| Height (cm)     | 163.52 (15, 161) | 161.98 (15, 161) |
| Male/female     | 37/17           | 36/18           |

The data are presented as mean (IQR, median), or number. IQR = Interquartile range

| Table 2: Spirometry and impulse oscillometry data in case and control according to mean (SD) |
|-----------------|-----------------|-----------------|
| Parameters      | Case (n = 54)   | Control (n = 54) |
| FVC (L)         | 3.33 (0.87)     | 3.76 (1.01)     |
| FEV₁ (L)        | 2.78 (0.75)     | 3.22 (0.87)     |
| FEV₁/FVC        | 83.40 (5.80)    | 86.32 (3.77)    |
| FEF 25-75 (L/s) | 2.68 (1.09)     | 3.63 (1.04)     |
| FEF 25-75/FVC   | 0.80 (0.24)     | 0.97 (0.15)     |
| R5 (kPa s/L)    | 0.37 (0.18)     | 0.30 (0.07)     |
| R25 (kPa s/L)   | 0.33 (0.14)     | 0.22 (0.06)     |
| X5 (kPa s/L)    | -0.08 (0.14)    | -0.11 (0.06)    |
| X25 (kPa s/L)   | 0.03 (0.20)     | 0.05 (0.03)     |
| Rₜₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚₑₚ_epi...
is different from the previous investigations, as it is the only study that has used the IO for evaluation of COPD patients’ offspring. All of the subjects who completed the questionnaire and the spirometry were nonsmokers.

The findings reported here are unlikely to be due to chance in view of the highly significant difference between the two population. The possibility of confounding has been diminished by matching for age, height, and sex. Although we cannot exclude residual confounding, for example, by industrial exposure, it would be unlikely to explain this magnitude of association. The most important issue is of potential bias in the measurement of pulmonary function in the two population.

Mechanical events in the respiratory tract begin with minor increments in airway resistance. An increase in driving pressures, caused by overuse of respiratory muscles, may mask these early stages of airway obstruction, especially in individuals with stronger muscles. Detection of these changes, therefore, needs the use of sensitive techniques.

Airway resistance is classically measured using body plethysmography. However, the IO provides measurements of airway resistance that correlate well with those at plethysmography both in healthy subjects and in patients with pulmonary disease. Using the IO, typical patterns of resistance and reactance have been recognized in different types of pulmonary diseases. For instance, obstruction of peripheral airways, such as in chronic bronchitis, is associated with increased resistance and decreased reactance at 5 Hz, and an increase in resonance frequency. Our findings suggest the presence of a dormant airway pathology expressed by increased resistance in relatives of COPD patients who have no respiratory complaints. Nearly half of COPD offspring had increased airway resistance with respect to our previous study on predicting the equation of the IO. Although these cases had lower FEV, FVC, and mean flow rates than healthy subjects, the reductions were not adequate to label the cases having pulmonary disease. However, IO revealed definite evidence of airway resistance in these cases. Patients with such subclinical abnormalities may be at greater risk of developing symptomatic lung disease in the future.

Supporting our findings, investigations performed by Mikamo et al. and Mori et al. showed that oscillometry parameters can predict the extent of pulmonary diseases such as emphysema and differentiate COPD from other lung disorders. However, we could not find any specific research similar to ours which evaluated airway resistance in offspring of patients with severe COPD.

We conclude that significant numbers of severe COPD offspring are suffering from a subclinical airway disease as evidenced by increased airway resistance. Taken together, this study demonstrates marked familial clustering of airflow obstruction in nonsmokers. These data also provide an assessment of the ability to recruit nuclear families for genetic studies after the identification of a proband with severe COPD. It is possible that factors such as childhood passive smoking, infections, or diet could interact with smoking to account for the familial aggregation of disease. Therefore, this study demonstrated increased airway resistance among the severe COPD offsprings. The IO may be a sensitive tool for detection of high risk subjects in families with COPD.

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Conflicts of interest
There are no conflicts of interest.

AUTHOR’S CONTRIBUTION
BA and MG carried out the design and coordinated the study, participated in most of the experiments, and prepared the manuscript. VBB provided assistance in the design of the study and carried out all the experiments. FS participated in most of the experiments and prepared the manuscript. All authors have read and approved the contents of the manuscript.

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