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Prevalence of airway reversibility in connective tissue disease-interstitial lung disease (CTD-ILD)

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***Abstract*---**Background: Spirometry is the most reproducible and objective measurement of airflow limitation. Improvement in FEV1 and/or FVC by 12% or 200ml after using bronchodilator is definitive of reversible airway disease. Several conditions like sarcoidosis predominantly involve the interstitium have nevertheless been associated with reversible airways obstruction. Connective tissue diseases (CTDs) form another important subgroup of interstitial lung disease (ILD). CTDs usually produce a restrictive pattern of lung involvement on spirometry, but might have unrecognized additional reversible airway obstruction. Seeking out and treating the latter components of disease may be crucial in optimizing lung function and alleviating the breathlessness that is common to the problem. Aim: The aim of this study is therefore to determine the post bronchodilator

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response in patients with connective tissue disease related interstitial lung disease (CTD-ILD) and thus potentially help improve quality of life by addressing the latter component by inhaled bronchodilator-steroid therapy. Methods: Consecutive patients with a confirmed diagnosis of CTD-ILD were identified in the out-patient clinics of our institute. CTD was diagnosed by a combination of clinical and serological parameters. ILD was confirmed by high resolution computed tomography (HRCT) images. Spirometry and diffuse capacity of carbon monoxide (DLCO) were performed on these patients as per the acceptability criteria of the American Thoracic Society (ATS) guidelines.[1] Results: Out of 22 patients enrolled in the study, 50%(n=11) patients showed post-bronchodilator reversibility on spirometry. The mean FEV1/FVC was 115± 15.52. The mean post bronchodilator FVC was 52.22 ± 20.18 and mean FEV1 was 64.81 ± 23.35. Conclusion: Not withstanding the relatively small numbers of patients enrolled in our study, it was possible to infer that reversible airway obstruction should be specifically sought in all CTD-ILD patients, and their treatment supplemented with inhaled steroid-bronchodilator combination therapy.

***Keywords*---**prevalence airway reversibility, CTD-ILD.

Introduction

Spirometry is an important tool in the assessment of lung function, particularly for the determination of airway reversibility to bronchodilator therapy. The physiological response of airways to bronchodilator therapy involves airway epithelium, nerves, mediators, and bronchial smooth muscles.[1] As per ATS guidelines, airways responsiveness is considered to be present when the improvement in forced expiratory volume in the first second (FEV_1) or in the forced vital capacity (FVC) is at least 200ml.[1] Connective tissue diseases significantly impact morbidity and mortality. CTD are a group of diseases with heterogeneous systemic features and immune-mediated multi-organ dysfunction. Lung involvement is a decisive contributor to the mortality in CTD, and is now the leading cause of death in Systemic Sclerosis (SSc)[2] and an important cause of death in rheumatoid arthritis (RA), even as overall mortality rates for the two are falling.[3]

ILD is a common component in patients with autoimmune myopathies, SSc, Sjögren's syndrome, RA and systemic lupus erythematosus (SLE), with estimated prevalence's of 40%, 30–40%, 40%, 10% and 12%, respectively.[4] It is important to keep in mind that ILD may be the only manifestation of a yet to be diagnosed CTD.[5] High-resolution computed tomography (HRCT) and pulmonary function tests (PFT) are excellent tools to evaluate and monitor lung involvement, and also have prognostic value. [6,7,8] The objectives of the study were to evaluate patients with CTD-ILD with restrictive disease for possible bronchodilator responsiveness; and to correlate the severity of ILD (as assessed by DLCO) with the presence of any airway obstruction that might be present.

Materials and Methods

This study is a prospective observational study undertaken in the Department of pulmonary medicine at Owaisi hospital and research centre in Hyderabad, India.

Inclusion Criteria

- Patients age 20 years and above
- Proven ILD (clinically and serologically)
- Spirometry showing restrictive pattern
- Pattern on CT scan consistent with interstitial lung disease.
- Patients with restrictive pattern having significant post- bronchodilator responsiveness underwent DLCO.

Exclusion Criteria

- Patients who had recovered from acute exacerbation of ILD (i.e, those who had received steroids with potential impact on airway function and consequently upon the spirometric assessment of the same), less than a month ago.
- Persons below 20 years of age
- Asthma history prior to diagnosis of CTD-ILD
- Persons with CVD, CAD and other lung diseases
- Smokers

Patients diagnosed with CTD-ILD attending the out-patient department of pulmonary medicine who satisfied the inclusion and exclusion criteria, participated in the study. A total of 22 consecutive patients with CTD-ILD were screened and consented for the study. Spirometric practices followed ATS guidelines;[1] the ATS criteria were also used for the categorizations of normal, obstructive and restrictive pattern on pulmonary function test. Patients were subjected to pre and post bronchodilator tests, and post bronchodilator response was considered to be significant if post-bronchodilator values showed improvement of minimum 200ml in FEV_1 and/or FVC.[1] Simultaneous with spirometry, these patients performed DLCO using single breath method. Ethical committee approval was taken for the study, and informed consent taken from all patients.

Results

A total of 22 patients were included in the study. Most of the patients were symptomatic, with a common complaint of dyspnea, for which PFT was indicated. 82% (n=18) of these patients were females, while 18% (n=4) were males. The mean age of CTD-ILD subjects who showed airway reversibility was 55.10 ± 13.55. All the subjects enrolled in study were non-smokers and did not otherwise fulfill the criteria for a diagnosis of chronic obstructive lung disease. None of the patients had history suggestive of asthma prior to being diagnosed as CTD-ILD. All subjects had a restrictive pattern on spirometry and an interstitial pattern on

HRCT scan; in all subjects, the latter which was attributed to the underlying ILD.

The mean FVC was 52.22 ± 20.18 and mean FEV1 was 64.81 ± 23.35 and FEV1/FVC was 115.42 ± 15.52. The mean DLCO of subjects with airway reversibility was 49.84 ± 20.78 of which about 50% had severe reduction on DLCO. [9]

Males	4 (18%)
Females	18 (82%)
Mean age of Asthmatic patients	55.10± 13.55
Mean age of Non-asthmatic patients	54.18 ± 13.27
Total patients age	54.18 ± 13.27

ASTHMATIC		NON ASTHMATIC	
DLCO%: 49.84±20.78		51.59±21.16	
FVC			
52.00±19.31	56.84±20.61	53.40±19.16	52.22±20.18
FEV1/FVC			
114.10±17.21	114.70±16.46	114.72±16.14	115.42±15.52
FEF >75%			
52.68±47.60	41.26±20.56	52.22±44.34	42.18±19.70
FEF 50-75%			
49.94±26.60	47.36±20.73	51.36±25.15	49.45±20.37
FEF 25-50%			
49.15±21.86	53.57±20.72	52.5±25.24	56.09±23.42
FEF<25%			
36.68±27.43	39.52±29.46	38.45±28.86	40.22±31.23
FEV1			
58.26±22.51	63.84±24.01	60.36±22.49	64.81±23.35

Discussion

Our study was aimed at identifying bronchodilator reversibility in a subset of patients with CTD-ILD. All these patients were inducted from the respiratory OPD, with the implication that they all had some form of pulmonary involvement, in this case, interstitial lung disease.The consecutive patients included in the study, all had low FVC (52.22± 20.18) and FEV1 (64.81±23.35) with a normal

FEV1/FVC which suggests that all the stations at fairly advanced interstitial involvement. These findings of obstruction were consistent with the study of Hyatt et al.[10] The bronchodilator response in CTD and particularly in CTD-ILD has not been thoroughly studied. Our study, which is possibly unique in this respect, examines the possibility. About 50% of subjects had post-bronchodilator reversibility, suggesting that a further improvement in the quality of life of such patients might be anticipated by treating this element.

Our study is limited by its relatively small sample size, and therefore the inability to characterise airflow limitation in each individual CTD independently. Different CTDs might be anticipated to produce their effects on the long and indeed on the airways in manner that might differ between the various CTDs and might be unique to a particular CTD. As well, due to the lingering effects of corticosteroids received in the more distant past (our study limited the patients to those who had not received corticosteroids for one month, minimum). It is conceivable that several more instances of reversible airway obstruction might have been missed on spirometry, thus actually underestimating the presence of reversible airway obstruction in this group of patients.

The other point of note is that although fully 50% of patients showed reversible airways obstruction as defined by post-bronchodilator FEV1and FVC criteria, none of these patients had shown an abnormal (obstructed) FEV1/FVC ratio to begin with. Although the combination of a normal FEV1/FVC ratio along with significant post-bronchodilator improvement in FEV1 and FVC (to the extent of fulfilling the definition of reversible airways obstruction) is not unusual of itself.[11] It certainly draws attention to the fact that not specifically looking for post-bronchodilator improvement in specific spirometric values would lead to missing this pattern.

Conclusion

Our study concludes that airways obstruction is an unrecognised and underestimated component of CTD-ILD. A reversible obstructive component should actively be sought on spirometers in patients with CTD-ILD, with the likely consideration that such patients might gain symptomatic relief with inhaled corticosteroid- bronchodilator therapy.

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