ORIGINAL RESEARCH PAPER

Pulmonary Medicine

BRONCHODILATOR REVERSIBILITY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

KEY WORDS: COPD. bronchodilator reversibility. GOLD

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ABSTRACT

Background: Although airflow obstruction in COPD is not fully reversible, patients can still exhibit clinically significant bronchodilator reversibility. This study assessed bronchodilator reversibility in COPD

Materials and methods: Spirometric parameters were measured before and after inhaled 400 µg salbutamol. Responses were classified using the American Thoracic Society (ATS)/European Respiratory Society (ERS) criteria and patients were classified as reversible and irreversible.

Result: There was a clear positive correlation between FEV_1 reversibility and FVC reversibility. FEV_1 increased significantly with bronchodilator in 25% of COPD patients, a response that was normally distributed. FVC reversibility was seen in 62.5% of COPD

Conclusion: COPD patients on the mild side of the severity spectrum differ from patients on the severe side regarding the association between their bronchodilator flow and volume responses.

Introduction:

A limited or absent bronchodilator response is used to classify COPD. A central feature of COPD is airflow obstruction that is not fully reversible, defined as a post bronchodilator FEV_1/ FVC ratio of < 0.70. Although airflow obstruction in COPD is not fully reversible, patients can still exhibit clinically significant bronchodilator reversibility , based on changes from pre bronchodilator values in FEV_1 and/or FVC. The FVC component is particularly important in patients with more severe COPD who have greater hyperinflation, as these patients often show clinically meaningful improvement in FVC without a significant FEV_1 response after bronchodilator treatment.Confusion exists surrounding the concept of bronchodilator reversibility because of the lack of a standardized definition and methodologies for assessing reversibility. This study was undertaken to assess the bronchodilator reversibility in COPD.

COPD is defined as a disease state that is characterized by a progressive and not fully reversible airflow limitation[1]. Expiratory flow response after administration of a bronchodilator is widely and frequently used as an indicator for the degree of reversibility of airflow limitation in patients with COPD [2-3]. In severe COPD, flow response after bronchodilator may almost be negligible [4,11]. Bronchodilator response in terms of lung volumes has been addressed by several authors, as well as the relationship between flow response and volume response[5-7]. A study in patients with severe COPD showed a significant correlation between flow and volume responses. Expiratory flow limitation promotes dynamic hyperinflation and increased work of breathing in patients with severe COPD[8,10]. Bronchodilator-induced lung deflation has been shown to increase ventilatory capacity and decrease respiratory discomfort, thereby increasing exercise endurance in patients with severe COPD[9]. Patients with moderate to severe COPD generally show a poor response to bronchodilator in terms of flow, but the response in terms of volume (including vital capacity) can be relatively good, which is probably a reflection of reduced hyperinflation[7,13]. Thus, it is likely that an increase of the expiratory volume after inhalation of a bronchodilator reflects reduced lung hyperinflation and decrease of functional residual capacity or end-expiratory lung volume[12,14]. So far studies that have reported on the relationship between expiratory flow and volume responses after administration of a bronchodilator in chronic obstructive pulmonary disease have been rather small in terms of population size.

Materials and methods:

This cross sectional observational study was conducted in the department of pulmonary medicine, Medical college, Thrissur in 120 patients with COPD who visits the OPD of pulmonary medicine. Inclusion criteria were COPD subjects aged 40 – 90 years with a smoking history of more than 10 pack-years with post-bronchodilator FEV_1/FVC ratio <0.7.Patients with asthma, malignancy, exacerbation COPD, ischemic heart disease, uncontrolled hypertension, heart failure were excluded. After careful history and physical examination pulmonary function test will be done. After administration of 400 g salbutamol pulmonary function test will be repeated. Post bronchodilator FEV_1/FVC ratio<0.7 was taken to confirm COPD. FEV_1 and FVC reversibility was assessed in comparison with pre bronchodialator pulmonary function test. Reversibility is assessed as per ATS/ERS guidelines and improvement in FEV_1or FVC of ≥12% and 200ml is taken as reversibility. Institutional ethical committee approval was obtained and informed consent was taken from all patients.

RESULTS

The clinical characteristics are given in table .1.

Table .1 Demographics and background characteristics

	Patients with COPD	COPD with reversibility	COPD without reversibility	p-value
Subjects n (%)	120	75 (62.5%)	45 (37.5%)	
Mean age (years)	64.6	64.8	64.3	0.856
Gender(M/F)	96(80%)/24(20%)	69(92%)/6(8%)	33(73%)/12(27%)	0.109
Smoking history	96(80%)	69 (92%)	33 (73%)	0.109
BMI kg/m^2	20.7	20.8	20.5	0.838
FEV_1 % (pred) Pre BD	43.3	38.6	51.2	0.014
FVC % (pred) Pre BD	62	57.7	69	0.034
FEV_1 % (pred) Post BD	49	45	55.73	0.038
FVC % (pred) Post BD	72.2	72.1	72.2	0.987
% change FEV_1 Post BD	16.7	21.4	9.04	0.042
% change FVC Post BD	17.9	27	2.9	0.001
FEV_1 change in ml Pre BD	130	154.8	88.7	0.075
FVC change in ml Post BD	273.3	375.6	102.7	0.001

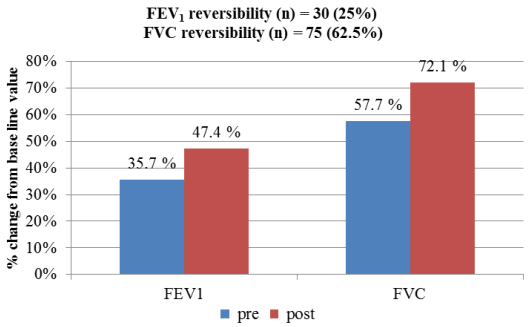

Figure 1: The relationship between % change and FEV1 and FVC pre and post salbutamol

Among 120 patients 62.5% (n=75) had volume reversibility and 25% (n=30) showed flow reversibility. Flow reversible group had mean FEV_1 change as 38.4 % and 273ml . Volume reversible group had FVC change as 27 % and 375.6 ml. In volume reversible group (n=75) flow reversibility was there in 30 (40%) and rest 45 (60%) had no flow reversibility. In volume reversible group with flow reversibility mean change in FEV_1 was 38.4 % and 273ml where as FVC change was 32.7 % and 470ml. In volume reversible group without flow reversibility the FVC change was 23.1% and 313 ml.

Discussion

As per the study result; FEV_1 reversibility with bronchodilator was seen in 25% and FVC reversibility was seen in 62.5% of COPD. This study assessed the differences in and associations between pre and post salbutamol flow (FEV_1) and volume (FCV) responses during routine spirometry reversibility testing in COPD. There is association between flow and volume response changes as COPD becomes more severe since there was a post bronchodilator change in FVC without a concomitant change of FEV_1 in severe stages of COPD. This suggests that the airway smooth muscle tone; which is the point of impact of all inhaled bronchodilators; is a major determinant of airway caliber at low, but not at high lung volumes[13]. The altered effect of lung inflation on airway caliber, due either to loss of lung elastic recoil or compression by emphysematous air spaces may explain the lack of sensitivity to bronchodilatation as assessed by changes in FEV_1 in the more severe stages of COPD. A practical implication of finding is that it is important to realise that patients with COPD even if non responders in terms of flow may benefit from bronchodilators because they can breathe at a lower lung volume due to reduced air trapping, notwithstanding the fact that they are still flow limited[15]. These more subtle physiological effects help to explain why changes in FEV_1 after a bronchodilator that fall within the between test reproducibility of the measurement can translate into the clinically relevant improvements in exercise capacity, health status, exacerbation frequency, and even in symptom intensity during exacerbations. Many patients with COPD show some improvement in FEV_1, FVC, or both, after a bronchodilator, and this response to treatment can reach the thresholds believed to represent reversibility. In fact, changes in end-expiratory lung volume after administration of a short-acting bronchodilator track changes in residual volume and the change in FVC, irrespective of GOLD grade. This contrasts with FEV_1 change which, as noted above, decreases in magnitude as the percent predicted pre-test value falls. Thus, change in FEV_1 is an indirect marker of the physiologically important effect of the bronchodilator, and as disease becomes more severe, the change in end-expiratory lung volume and FEV_1 become less closely related. Moreover, this differential effect on FEV_1 and FVC can produce a seemingly paradoxical decrease of FEV_1/FVC ratio. This discrepancy results in some patients having an isolated FVC response which has been associated with emphysema as was seen in the NETT data. Reversibility testing might be more helpful in truly treatment-nad've individuals, although it seems likely that the same issues of between-test variability in lung function will still apply. Patients with reversible COPD were more likely to report a response to oral corticosteroids than were patients without reversible COPD[16]. This form of response testing was not a specific marker of disease progression on longer term follow up[17]. Reversibility status has been linked to specific chromosomes in genetic studies of COPD[18]. Patients who never responded were more likely to exacerbate in the 2 years of follow up.

Conclusion:

This study reveals the current data on post bronchodilator reversibility to short acting beta agonist salbutamol. Significant reversibility was seen in 62.5% patients with COPD as per ATS/ERS criteria There was a clear positive correlation between FEV_1 reversibility and FVC reversibility. FEV_1 increased significantly with bronchodilator in 25% of COPD patients, a response that was normally distributed. FVC reversibility was seen in 62.5% of COPD. Percentage change in FEV_1 decreased as the GOLD stage became more severe where as percentage change in FVC changed in the opposite direction more in severe stage compared with mild stage.

Conflicts of interest: nil

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