

# BRONHODILATOR RESPONSE TO NEBULIZED SALBUTAMOL IN ELDERLY PATIENTS WITH STABLE C.O.P.D

Mohammad Hussain Khan, Arshad Javaid

Department of Pulmonology, Post graduate Medical Institute  
Lady Reading Hospital Peshawar, Pakistan

## ABSTRACT

**Objective:** To assess the response of elderly patients with stable COPD to beta-2 agonist.

**Material and Methods:** This interventional study was conducted in Pulmonology unit, Lady Reading Hospital, Peshawar. Patients were recruited after considering inclusion and exclusion criteria. A detailed history and clinical examination performed. On first day, baseline pulmonary function test (P.F.T) (F.E.V 1, F.V.C, F.E.V 1/F.V.C, P.E.F.R) was taken. Then 3 ml normal saline (placebo) was administered via cho-neb nebulizer. P.F.T measurements were repeated after 15, 30, 60 and 120 minutes. The best of three readings was recorded. On next day, the same protocol was applied except that placebo was replaced by nebulized salbutamol 5 mg (1 ml) plus 2 ml normal saline was administered via nebulizer.

**Results:** Out of 40 patients fulfilling entry criteria 30 completed the study. Age range was from 60-80 years. The mean baseline for F.E.V1 and F.V.C were 0.52 and 0.76 respectively. There was no significant difference in the mean baseline values on two days. The results expressed as mean and peak percentage changes about the baseline are shown in tabular and graphical form. 60 % patients responded to salbutamol and 25 % to normal saline. Analysis of variance comparing change in F.E.V1 between salbutamol and normal saline revealed highly significant drug effect ( $P < 0.01$ ). The drug effect comparing changes in F.V.C was statistically not significant ( $P > 0.05$ ).

**Conclusion:** Salbutamol can produce useful bronchodilatation in elderly patients with stable COPD which can be readily assessed using spirometry.

**Key words:** COPD, Beta 2 Agonist, elderly population.

## INTRODUCTION

COPD (Chronic Obstructive Pulmonary Disease) is a disease of the airways and lungs characterized by a chronic inflammatory process, in which patients develop progressive loss of lung function (e.g. fall in FEV1) and symptoms of breathlessness some times associated with chronic sputum production, leading to a reduction in quality of life measure.<sup>1</sup>

There is a wide spectrum of disease, recurrent exacerbations and a higher risk of death. The categorization of COPD severity has been described in the *Global Initiative for Chronic Obstructive Lung Disease* (GOLD) based essentially on the level of airflow obstruction measured with FEV1 and on the presence of symptoms.<sup>2</sup> In most cases, cigarette smoking is directly linked to the development of COPD,

although risk factors may also be involved such as environmental air pollution and respiratory infections.

COPD is a common condition affecting 4-9 % of the adult population.<sup>3</sup> COPD is a major cause of morbidity in old age, affecting approximately 16 % of patients of over age of 60-65 years. WHO has estimated the worldwide prevalence of COPD in 1990 to be 9.34/1000 in men and 7.33/1000 in women in all ages and that it must be considerably higher in old age groups. WHO predicts that between 1990 and 2020, COPD will rise from the 12<sup>th</sup> leading cause of disability to the 5<sup>th</sup> position and to become 3<sup>rd</sup> commonest cause of death.<sup>4</sup>

Treatments for COPD have remained purely on a symptomatic basis: relief of symptoms of breathlessness through reducing airflow

## MEAN VALUES AND % IMPROVEMENT FOR FEV1

| Time(min) | FEV1       |               |         |               |
|-----------|------------|---------------|---------|---------------|
|           | Sulbutamol | % Improvement | Placebo | % Improvement |
| 0         | 0.52       | 0             | 0.52    | 0             |
| 15        | 0.70       | 18            | 0.57    | 5             |
| 30        | 0.75       | 23            | 0.58    | 6             |
| 60        | 0.80       | 28            | 0.64    | 12            |
| 120       | 0.76       | 24            | 0.60    | 8             |

Table 1

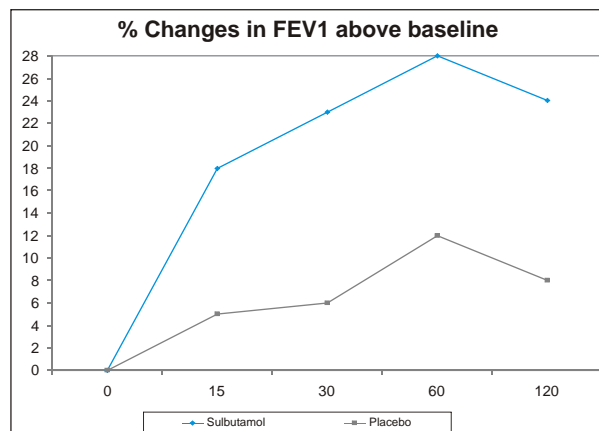


Fig 1

obstruction, relying mostly on the use of inhaled bronchodilator therapy including B2 adrenergic agonists and anticholinergics. The recent introduction of long acting B2 agonists (LABA) and long acting anticholinergics (LAA) has led to an improvement in the management of patients with COPD, allowing for more sustained bronchodilation and symptom relief<sup>5</sup>. The utility of inhaled corticosteroid therapy in COPD, in contrast to its well established use in asthma, remains somewhat controversial.

COPD related mortality has continued to increase in general population. Approximately 2.7 million deaths from COPD occurred in 2000, half of them in the Western Pacific Region, with the majority of these occurring in China. COPD is now characterized by an abnormal inflammatory response of lungs to noxious particles or gases. In addition, there seem to be an abnormal and insufficient tissue repair to counteract the destructive effects of cigarette smoke accompanying inflammation. The inflammation persists even after smoking cessation. Altogether, this results in epithelial changes, airway wall fibrosis and emphysematous lesions in lung parenchyma.<sup>7,8</sup> There is increasing evidence that exacerbations of COPD are inflammatory in their pathogenesis. It has been shown that exacerbations associated with symptomatic cold are accompanied by greater levels of airway inflammation.<sup>9</sup>

There has been considerable controversy concerning the benefits of treatment with B2 adrenergic receptor agonists. Several studies have been performed with varying results.

The present study was aimed to assess the response of elderly patients with stable COPD to beta-2 agonist.

### MATERIAL AND METHODS

This interventional study was carried out in Pulmonology unit, Lady Reading Hospital, Peshawar. Patients having respiratory symptoms were referred to this teaching hospital from all over province.

#### Inclusion criteria:

1. Clinically stable COPD patients
2. Age range 60-80 years
3. Forced expiratory volume in 1st second (FEV1) value less than 75 % of predicted
4. Able to perform spirometric test
5. Out patient chest clinic (OPD), case

#### Exclusion criteria was followed as;

1. Past history of asthma
2. Short term or seasonal variation in breathlessness
3. Severe non-respiratory physical disability
4. Attack of cardio respiratory illness less than 6 weeks

Consent was taken from these patients after briefing the protocol of study. A standardized history of respiratory symptoms was obtained. Relevant clinical examination performed. Dynamic lung volume ventilation studies arranged (F.E.V 1, F.V.C, F.E.V 1/F.V.C, P.E.F.R). On first day, base line P.F.T (F.E.V 1, F.V.C, F.E.V 1/F.V.C, P.E.F.R) was taken. Then 3 ml normal saline (placebo) was administered via cho-neb nebulizer.

P.F.T measurements were repeated after 15,30, 60 and 120 minutes. The best of three

## MEAN VALUES AND % IMPROVEMENTS FOR FVC

| Time(min) | FCV        |           |         |           |
|-----------|------------|-----------|---------|-----------|
|           | Sulbutamol | % Improve | Placebo | % Improve |
| 0         | 0.76       | 0         | 0.76    | 0         |
| 15        | 0.86       | 10        | 0.79    | 3         |
| 30        | 0.91       | 15        | 0.81    | 5         |
| 60        | 0.93       | 17        | 0.85    | 9         |
| 120       | 0.89       | 13        | 0.83    | 7         |

Table 2

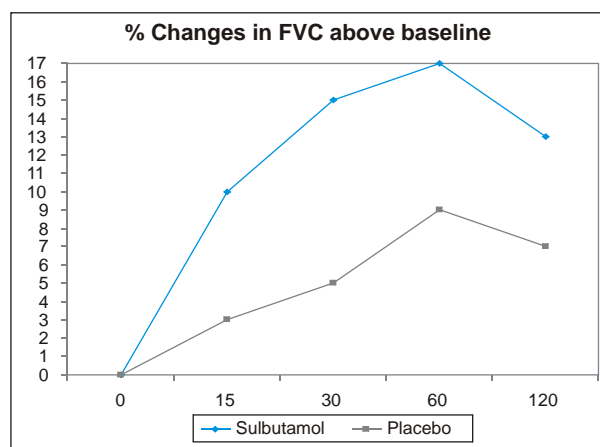


Fig 2

readings was recorded. On next day, the same protocol was applied except that placebo was replaced by nebulized salbutamol 5 mg (1 ml) plus 2 ml normal saline (total 3 ml) was administered via nebulizer.

## RESULTS

We recruited 40 patients from out-patient chest clinic for this study who fulfilled the criteria for entry. Among them, 10 patients did not return back on the next day for tests. The study was therefore, completed on 30 male patients. Age range was 60-80 years.

Patients presented with chronic cough and expectoration lasting for years. All were ex-smokers. Type of smoke inhaled was cheelum (huqqa) in 90 % cases while 10 % had habits of cigarette smoking. Duration of smoking was variable but was not less than 10 years in each case. All subjects were able to perform spirometry satisfactorily. The mean base line for F.E.V1 and F.V.C were 0.52 and 0.76 respectively.

There was no significant difference in the mean base line values on two days. The results expressed as mean and peak percentage changes about the base line are shown in tables 1 & 2 and figures 1 & 2. 60 % patients responded to salbutamol and 25 % to normal saline. Analysis of variance comparing change in F.E.V1 between

salbutamol and normal saline revealed highly significant drug effect ( P less than 0.01). The drug effect comparing changes in F.V.C was not impressive and statistically not significant (P more than 0.05 ).

## DISCUSSION

Chronic Obstructive Pulmonary Disease (COPD) is an important and growing cause of morbidity and mortality world wide.<sup>2,6,10</sup> WHO Global Burden of Disease Project<sup>2,6</sup> estimated that COPD would be the fifth leading cause of death world wide by 2020. The growing burden of COPD is partly due to ageing of world population and partly to the continued use of tobacco, which is the most important risk factor for this disease.<sup>2,6</sup> COPD has considerable importance on the quality of life in those who suffer. COPD has been the focus of recent reviews in the Lancet including one from 2003 by Claverley and Walker,<sup>9</sup> and another published in 2004 by Paules and Rabe.<sup>11</sup>

The working definition of COPD, as noted in 2006 update of Global initiative for obstructive lung disease (GOLD) guideline, is that COPD is a preventable disease with some significant extra pulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases.<sup>12</sup> The airflow limitation or obstruction that happens in COPD is caused by a mixture of small airway disease, parenchymal destruction (emphysema) and in many cases, increased airway responsiveness.<sup>12,13</sup> The frequency of the illness defined objectively by spirometry has now been appreciated although over interpretation of the term irreversible airflow obstruction has encouraged the view that nothing can be done to improve it.<sup>14,15</sup> Although present treatments have limited effects, the benefit of even modest improvements in lung function in people with severe disease is now recognized.<sup>13</sup> Bronchodilator reversibility as classified by American Thoracic

Society and GOLD criteria is a change in FEV1 that is greater than 12% of baseline and encompasses an absolute change of 200 ml.ERS<sup>2</sup> criteria defined it as a change in FEV1 that is greater than 9% of the value predicted for that person.<sup>13</sup> If a base line lung function is relatively well preserved, small changes in FEV1 after taking bronchodilator will probably not meet the threshold relative to the baseline for patients to be classified as having asthma. When lung function is severely reduced in advanced COPD, similar changes in lung function can lead to an erroneous diagnosis of asthma. The identification of so called isolated volume responders who show a clinically important reduction in forced Expiratory Vital Capacity(FVC) with a small change in FEV1 is an attractive notion, but so far we know little about how predictive, such results are or how they can be reproduced. To date, bronchodilator has been a poor predictor of short term improvement in exercise ability or of other clinical outcomes such as exacerbation frequency or health status.<sup>16,17</sup> As we know major functional lesion of disease is airway narrowing. Pharmacological approach that appears to diminish airway narrowing is beta 2 agonist, which reduces the severity of patient to bronchoconstrictor stimuli. This optimizes the bronchodilator response and so is of considerable importance in these patients. Tanden et al have shown that beta 2 agonist as bronchodilator therapy is effective in keeping patient symptom free, in partially reversible COPD cases.<sup>18</sup> Anderson et al studied the effect of controlled-release salbutamol in non-reversible COPD patients and found slight improvement in lung function. Thus limited clinical benefit is still achievable in non-reversible COPD.<sup>19-22</sup> Studies result suggest that ageing process is accompanied by decline in beta 2 receptor function in the airways of patients with COPD.<sup>23</sup>

This study demonstrated mean percentage improvement of reversibility test with salbutamol. Improvement in lung function (F.E.V1) is statistically highly significant.

Risk of developing tolerance or tachyphylaxis to beta 2 agonist is diminished by addition of corticosteroids.<sup>24-26</sup>

## CONCLUSION

This study demonstrated that salbutamol can produce useful bronchodilatation in elderly patients with stable COPD which can be readily assessed using spirometry.

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**Address for Correspondence:****Dr.Mohammad Hussain Khan**

Associate Professor

Gomal Medical College, D.I.Khan,

NWFP, Pakistan.

E-mail: drhussainbabar@gmail.com