# Efficacy of Salbutamol in Mixed Obstructive and Restrictive Pattern Spirometry

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## ABSTRACT

**Background**

Salbutamol is a short acting $\beta_2$ agonist bronchodilator most commonly used for management of asthma and chronic obstructive pulmonary disease. Besides the disease state, it is also used for bronchodilator reversibility in spirometry. The spirometry reading show one of the four patterns i.e. normal, obstructive, restrictive and combined or mixed (obstructive-restrictive).

**Objective**

To determine the efficacy of salbutamol in mixed obstructive and restrictive pattern spirometry.

**Method**

A descriptive cross sectional study was conducted at Nepal Medical College and Teaching Hospital (NMCTH) for a period of 9 months. A total of 70 patients who presented with symptoms of respiratory disease in medicine outpatient department (OPD) in which spirometry was performed were selected. Of the 70 patients, 35 with mixed pattern spirometry were selected as cases and remaining 35 with normal spirometry were selected as control. After taking informed consent, spirometry parameter were measured before and after salbutamol therapy. Data was collected from medicine department, pulmonary function test (PFT) unit. All the data were entered in statistical package for social sciences (SPSS version 20) and Forced expiratory volume in first second ($FEV_1$), Forced vital capacity (FVC), $FEV_1$/FVC and Peak expiratory flow rate (PEFR) were analyzed.

**Result**

There was significant difference ($p<0.05$) in spirometry parameters (i.e. $FEV_1$, FVC, PEFR) when after salbutamol therapy was compared from before therapy. Statistical significance was also seen in percentage change in spirometry parameter (i.e. $\%FEV_1$ change, %FVC change, % change in ratio of $FEV_1$/FVC and %PEFR change) between case and control groups.

**Conclusion**

Salbutamol is an effective bronchodilator in mixed pattern or combined obstructive-restrictive lung disease.

## KEY WORDS

*Bronchodilation, mixed obstructive and restrictive lung pattern, salbutamol, spirometry*

## INTRODUCTION

Salbutamol is a short acting $\beta_2$ agonist bronchodilator most commonly used for management of asthma and chronic obstructive pulmonary disease (COPD).[1-3] Although salbutamol is an effective treatment for acute exacerbation, its use is associated with undesirable side effects like tremor, tachycardia and hypokalemia.[4] It is also known by its other name "albuterol".[5] Besides the disease state, salbutamol is used in spirometry/pulmonary function test for bronchodilator reversibility.[6]

A spirometer can be used to determine how well the lung receive, hold and utilize air.[7] They are also used to monitor and determine the severity of lung disease and to determine whether the lung disease is restrictive (decreased airflow) or obstructive (disruption of airflow). The spirometry reading usually show one of the four patterns: normal, obstructive, restrictive, combined or mixed (obstructive and restrictive).[7]

Obstructive lung disease include diseases like asthma and COPD.[8] Restrictive lung diseases can be produced by a number of defects: increased elastic recoil (interstitial lung disease), respiratory muscle weakness (myesthnia gravis), mechanical restrictions (pleural effusion) and poor effort.[9] Mixed obstructive and restrictive lung disease is common in clinical practice. It is more commonly caused by a mixture of parenchymal and non-pulmonary disorder than by single pulmonary entity.[10]

## METHODS

A descriptive cross sectional study was conducted in Department of Medicine, NMCTH from 20th March 2016 to 20th December 2016. Informed consent was taken from all the patients regarding the procedure. Confidentiality and anonymity of the patients was assured and maintained. Ethical approval was taken from the Research and Ethical Sub Committee (RESC) of NMCTH.

A total of 70 patients who presented with symptoms of respiratory disease in medicine OPD in which spirometry was performed were selected. Of the 70 patients, 35 patients with mixed obstructive-restrictive pattern were selected as cases and remaining 35 patients had respiratory symptoms but no airway diseases were selected as control. The spirometer used was SCHILLER SP-26C. A qualified pulmonary technologist performed spirometry in patients referred from OPD. The patients were instructed and were asked to perform spirometry at least three times to observe $FEV_1$, FVC, $FEV_1$/FVC ratio and PEFR. The best values were considered for analysis. After completion of spirometry, the same patient was given salbutamol 1 ml (5 mg) mixed with 2 ml of normal saline via nebulizer. Spirometry was performed again in the same patient immediately after administration of drug.

The spirometry parameters ($FEV_1$, FVC, $FEV_1$/FVC, PEFR) after salbutamol therapy were compared from before therapy for case and control groups. Similarly, another spirometry parameters (%$FEV_1$ change, %FVC change, %$FEV_1$/FVC change, %PEFR change) were compared between case and control group. All the data were entered in SPSS version 22 and spirometry parameter were analyzed using paired t-test and independent sample t-test. P-value less than 0.05 was considered as statistically significant.

## RESULTS

Among the 35 patients who were selected as cases, 27 were females and 8 were males. Among the 35 patients who were selected as controls, 22 were females and 13 were males. In our study, mixed obstructive-restrictive pattern was seen in patients with age ranging from 43-88 years. Among these patients, mixed obstructive-restrictive pattern was predominant in the age group 60-69 years followed by 70-79 years.

There was significant difference ($p<0.05$) in spirometry parameters (i.e. $FEV_1$, FVC, PEFR) among patient before and after salbutamol therapy. However, there was no significant difference in $FEV_1$/ FVC ratio.

**Table 1.** Spirometry parameters of patients

| Spirometry parameter | Mean | Std. Deviation | p value |
|---|---|---|---|
| $FEV_1$ before | 42.26 | 12.969 | <0.05 |
| $FEV_1$ after | 49.57 | 14.425 | |
| FVC before | 50.14 | 10.325 | <0.05 |
| FVC after | 62.49 | 10.912 | |
| $FEV_1$/FVC before | 76.20 | 11.499 | <0.05 |
| $FEV_1$/FVC after | 72.69 | 14.313 | |
| PEF before | 40.06 | 16.290 | <0.05 |
| PEF after | 49.37 | 19.555 | |

**Table 2.** Spirometry parameters of control group

| Spirometry parameter | Mean | Std. Deviation | (paired t-test) p value |
|---|---|---|---|
| $FEV_1$ before | 115.77 | 26.879 | p value |
| $FEV_1$ after | 125.69 | 28.978 | |
| FVC before | 110.03 | 20.39 | <0.05 |
| FVC after | 118 | 21.035 | |
| $FEV_1$/FVC before | 101.46 | 9.284 | 0.240 |
| $FEV_1$/FVC after | 102.51 | 7.732 | |
| PEF before | 116.23 | 22.12 | <0.05 |
| PEF after | 129.54 | 26.317 | |

Percentage change in spirometry parameters (i.e. %$FEV_1$ change, %FVC change, % change in $FEV_1$/FVC and %PEFR change) were compared between case and control groups, which was statistically significant ($p<0.05$).

**Table 3. Percentage change in Spirometry parameter for case and control**

| Interpretation | | Mean | Std. Deviation | (independent sample t-test) p value |
|---|---|---|---|---|
| % $FEV_1$ change | case | 19.20 | 15.237 | <0.05 |
| | control | 8.54 | 6.026 | |
| % FVC change | case | 25.86 | 13.789 | <0.05 |
| | control | 7.34 | 5.127 | |
| % $FEV_1$/FVC change | case | -4.06 | 11.122 | <0.05 |
| | control | 1.31 | 5.465 | |
| % PEF change | case | 25.29 | 21.382 | <0.05 |
| | control | 11.60 | 10.536 | |

## DISCUSSION

Dyspnea, a breathing difficulty associated with lung, in active age and adult age have been reported as a national burden around the world particularly in developing nations.[11-13] In developed countries, cigarette smoking remains the major cause behind respiratory diseases, but in developing countries like Nepal besides cigarette smoking; increasing construction, combustion fuel, air pollution, incrementing number of houses, decrementing forest areas has incorporated extra contribution to perpetual respiratory disease.[14-17] However, in the rural areas, exploitation of fire wood for cooking remains the major cause for respiratory diseases in women.[18,19] In spite of knowing all these factors, we still have not found a solution but instead are relying more on pharmacological preparations for its management. This havoc in society has spared none in our society. From small children to elderly men, all have suffered from some kind of respiratory illness then and now.[20] This illness would not have persisted in our society only if we had been aware of future consequences that our progeny might have to face later in their life. Health education routinely conceded in all countries of globe from the direction of respective health ministry to minimize lung disease.[21] This health education is very important for Nepalese population because majority of this disease burden were found in low socioeconomic class in all parts of the country.[22,23] They need to know about the predisposing risk factors such as tobacco smoke, exposure to dusts, fumes from burning fuel which can contribute to respiratory infections, heart problems, lung cancer. Although the current solution might be home therapy with steam inhalation or use of prescription/non-prescription drugs, both have their own consequences.[24]

Pharmaceutical preparation that are available in the market have one or more adverse drug reaction.[25] In spite of these adverse drug reactions, medicines are effective in managing respiratory diseases.[21] There are various pharmaceutical preparations for respiratory diseases available in the market among which salbutamol in the one.[26] It produces immediate bronchodilation relieving patient of bronchospasm. Being a selective $\beta_2$ receptor agonist, it binds to this receptor and via G-stimulatory protein coupled receptor that activate adenylcyclase enzyme which in turn catalyze adenosine triphosphate (ATP) to cyclic adenosine monophosphate (cAMP), it causes bronchodilation.[27,28] The adverse effect of $\beta_2$ agonist are minimal when they are inhaled and this is preferred route of their inhalation.[29,30] Administration of oral route is associated with muscle tremor due to stimulation of $\beta_2$ receptor in the skeletal muscle that produce glycogenolysis.[31,32] It can also produce tachycardia due to stimulation of chronotropic $\beta_2$ receptor and in high dose $\beta_1$ receptor in heart.[28] Continued use of these agents usually result in desensitization/ down regulation of $\beta_2$ receptor that result in diminished responsiveness.[33,34] However, in certain respiratory diseases like COPD, salbutamol is less effective.[35,36] In COPD patients, anticholinergics are more effective because they reduce the excess cholinergic activity.[37-39] It is because of its immediate onset of action, salbutamol is used in this study.[40,41] Salbutamol can be administered either orally or by inhalation. However, selectivity of action is less when the drug is given orally. These can also be given by IV or IM route.[42] When inhaled, these drugs produce effective bronchodilation with minimal cardiac stimulation.[28] Inhaled short acting $\beta_2$ agonists are normally the drugs of choice for managing acute bronchospasm because they are less likely to activate other adrenoceptors.[41] Inhaled salbutamol produce bronchodilation within 5 min and the action last for 2-4 hours. It is therefore suitable for terminating the attack of bronchospasm but not suitable for prophylaxis.[43]

Based on the interpretation of spirometry, they can be classified as obstructive, restrictive or mixed pattern i.e. combination of both obstructive and restrictive pattern.[44] In this study, mixed pattern of lung disease was predominant in female. Although it is not known how gender influence obstructive and restrictive lung disease, other studies have reported that physiologic and psychologic impairment may be the cause and requires deeper insight.[45] This mixed pattern was present in 60-80 years of age group that was similar to the previous study.[46] According to their study, as the body changes with age, it will have an impact on the entire respiratory system. Structural changes, change in muscle function, pulmonary immunologic function could lead to obstructive and restrictive lung disease in elderly.[46]

Spirometry, a physiological test, is commonly used for evaluation of pulmonary function. One important application of spirometry is to show responsiveness of airways to bronchodilator administration.[47] Bronchodilator response is usually performed in subjects with obstructive spirometry pattern but recent studies has suggested that bronchial reversibility may be accompanied by normal, restrictive and mixed pattern of spirometry. The mixed pattern represents airway obstruction with lung hyperinflation.[47]

In this study, we assessed bronchodilator response in mixed pattern of spirometry. There was significant difference in

pattern before and after salbutamol therapy for spirometry parameters like $FEV_1$, FVC and PEFR. However, the ratio of $FEV_1$/FVC before and after the therapy was not significant. The reason could be improvement in $FEV_1$ and FVC by equal proportion. In order to improve accuracy of the study, the data were compared between cases and control groups where percentage change in spirometry parameter (%$FEV_1$ change, %FVC change, %$FEV_1$/FVC change and %PEFR change) were accounted. We found statistically significant difference in all the above mentioned parameters i.e. not only there was difference in $FEV_1$, FVC, PEFR but also the ratio of $FEV_1$/FVC. Hence, salbutamol is efficacious in mixed pattern interpretation by spirometry. This result was similar to a study conducted by Mehrparvar et al.[47] According to that study, patients with mixed pattern had the highest frequency of response to bronchodilator.[47] Thus it can we concluded that salbutamol is an effective bronchodilator in mixed pattern obstructive-restrictive lung disease.

Nepal is predominantly a rural country. It is difficult to comment on the true efficacy of salbutamol as this was a hospital based study and the subset of patients were mostly form urban community which not only limited the sample size but also focused more on monocentric study with shorter duration. Therefore, this study was not able to identify the extent of problem in the rural population. In order to determine the efficacy of salbutamol, a larger, community based study should be conducted.

## CONCLUSION

Mixed obstructive and restrictive lung diseases are common cause of mortality and morbidity which requires preliminary assessment and diagnosis. Although there are many more drugs that can be used, salbutamol is found to be effective bronchodilator in mixed pattern obstructive-restrictive lung disease.

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