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Effect of Combined Nebulized Salbutamol and Ipratropium Bromide on Spirometric Parameters in Acute Exacerbation of COPD: A Comparative Study

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Abstract **Original Research Article**

Background: Acute exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD) is associated with worsening airflow limitation and decline in respiratory function. Improvement of spirometric parameters is an important therapeutic goal during exacerbation. Combined nebulized salbutamol and ipratropium bromide therapy may provide enhanced bronchodilation compared with single-agent therapy. This study aimed to evaluate the effect of combined nebulized salbutamol and ipratropium bromide on spirometric parameters in patients with AECOPD. ***Objective:*** To evaluate the effect of combined nebulized salbutamol and ipratropium bromide on spirometric parameters in patients with acute exacerbation of COPD. ***Methods:*** This hospital-based comparative study was conducted in the Department of Respiratory Medicine of a tertiary care hospital in Bangladesh. Patients diagnosed with acute exacerbation of COPD were included according to predefined inclusion and exclusion criteria. Spirometric parameters including FEV1, FVC, FEV1/FVC ratio, and PEFR were measured before and after nebulized therapy. Patients receiving combined salbutamol and ipratropium bromide nebulization were compared with those receiving salbutamol alone. Statistical analysis was performed using SPSS version 23. ***Results:*** Significant improvement in spirometric parameters was observed after bronchodilator therapy in both groups. However, the combination therapy group demonstrated greater improvement in FEV1, FVC, and PEFR compared with the salbutamol-only group. The improvement in airflow limitation was statistically significant in patients receiving combined nebulization therapy. ***Conclusion:*** Combined nebulized salbutamol and ipratropium bromide significantly improves spirometric parameters in patients with acute exacerbation of COPD and provides better bronchodilation than salbutamol alone. The combination regimen may therefore be beneficial in routine management of AECOPD patients.

Keywords: Acute Exacerbation of COPD, Salbutamol, Ipratropium Bromide, Spirometric Parameters, Bronchodilator Therapy.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a chronic progressive respiratory disorder characterized by persistent airflow limitation and chronic inflammatory changes in the airways [1]. It is one of the leading causes of morbidity and mortality worldwide and imposes a significant healthcare burden [2]. Clinical manifestations of COPD include chronic cough, sputum production, wheezing, chest tightness, and progressive dyspnea [2]. Acute exacerbation of COPD is associated with worsening airflow limitation and accelerated decline in pulmonary function.

Spirometry is the gold standard method for diagnosis and assessment of COPD severity [3]. Parameters such as Forced Expiratory Volume in one second (FEV1), Forced Vital Capacity (FVC), FEV1/FVC ratio, and Peak Expiratory Flow Rate (PEFR) are essential for evaluating airflow obstruction and monitoring therapeutic response. Improvement of spirometric parameters is therefore an important goal during management of acute exacerbation.

Inhaled bronchodilators remain the foundation of pharmacotherapy for COPD because they relieve symptoms, decrease exacerbation frequency, and improve quality of life [4-7]. These agents also improve airflow and reduce hyperinflation [8-12]. Salbutamol, a short-acting β2 agonist, acts by relaxing airway smooth muscle, whereas ipratropium bromide, a short-acting anticholinergic, inhibits vagally mediated bronchoconstriction [13]. Because these drugs have different mechanisms of action, combined therapy may produce additive bronchodilator effects and greater improvement in lung function.

Nebulized bronchodilator therapy is widely used in hospitalized patients with acute exacerbation of COPD because it provides rapid symptomatic relief. Previous studies have demonstrated that the addition of ipratropium bromide to nebulized β2 agonists is beneficial in COPD management [14-16]. Improvement in spirometric parameters following combination therapy may indicate superior bronchodilator efficacy compared with β2 agonist monotherapy. However, evidence regarding the comparative effect of combined nebulized salbutamol and ipratropium bromide on spirometric indices among Bangladeshi COPD patients remains limited. Therefore, this study was conducted to evaluate the effect of combined nebulized salbutamol and ipratropium bromide on spirometric parameters in acute exacerbation of COPD.

Objective

General Objective

- To evaluate the effect of combined nebulized salbutamol and ipratropium bromide on spirometric parameters in patients with acute exacerbation of COPD.

Specific Objectives

- To assess changes in spirometric parameters following combined nebulized salbutamol and ipratropium bromide therapy in acute exacerbation of COPD.
- To compare spirometric improvement between nebulized salbutamol alone and combined nebulized salbutamol with ipratropium bromide.
- To determine the duration of hospital, stay between patients receiving nebulized salbutamol alone and those receiving combined nebulized salbutamol and ipratropium bromide.

MATERIAL AND METHOD

This comparative cross-sectional study was carried out in the Medicine Units of Rajshahi Medical College Hospital, Rajshahi, over a period of six months from July 2017 to December 2017. The study population consisted of patients admitted with acute exacerbation of Chronic Obstructive Pulmonary Disease (COPD). A total of 100 consecutive patients fulfilling the inclusion and exclusion criteria were enrolled by purposive sampling method. Inclusion criteria included clinically diagnosed COPD patients with acute exacerbation, age more than 40 years, both male and female patients, and willingness to provide informed written consent. Patients with severe non-respiratory physical disability and critically ill patients requiring ICU support were excluded from the study. Data were collected through detailed history taking, physical examination, and spirometric measurements using a predesigned questionnaire and data collection sheet after obtaining informed written consent from each patient. On admission, patients were purposively allocated to receive either solution-1 consisting of nebulized salbutamol 5 mg (5 ml) four times daily or solution-2 consisting of nebulized salbutamol 5 mg (5 ml) plus ipratropium bromide 500 µg (2 ml) four times daily. The medications were administered using an air-driven nebulizer at a flow rate of 8 L/min until the nebulizer chamber became dry, and the combination therapy was administered as a mixed solution. Other medications were prescribed according to the attending physician's usual management plan. Spirometric parameters (best of three attempts) were measured at 1 hour, Day 1, Day 3, and on the discharge day. A simple subjective score was also recorded, where patients were asked whether they felt better, worse, or the same compared to the previous day. To ensure treatment uniformity, coded medication packages were prepared and dispensed by the investigator himself. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 16. Descriptive and inferential statistical methods including t-test, chi-square test, ANOVA test, frequency distribution, percentage, mean, and standard deviation were applied. The results were presented in tables, figures, and diagrams. Ethical issues were properly maintained throughout the study. All participants were informed regarding the purpose and nature of the study and assured about confidentiality of information prior to obtaining written informed consent.

RESULT

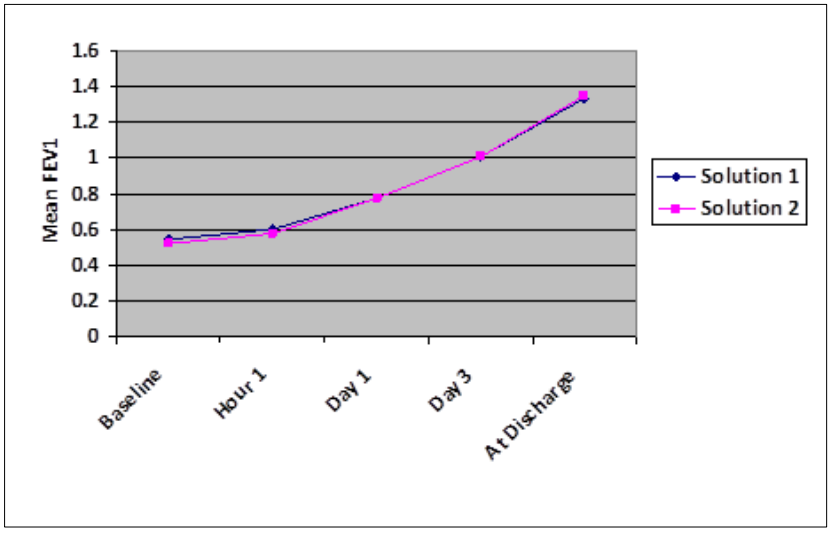

Figure 1: Mean change in FEV1 over time (N=100)

No significant difference was observed between solution-1 & solution-2 groups in FEV1 at baseline(t=0.888,df=98,p>0.05),at 1 hour (t=0.797,df=98,p>0.05), at day 1(t=-0.021,df=98,p>0.05),at day 3 (t=-0.051,df=98,p>0.05) and during discharge (t=-0.833,df=98,p>0.05).

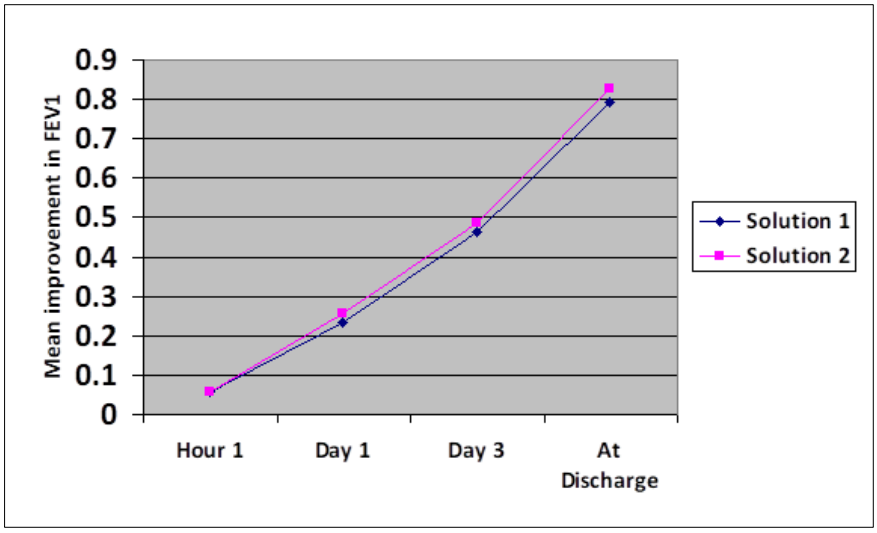

Figure 2: Mean improvement in FEV1 over time (N=100)

There was no significant difference in improvement between solution-1 & solution-2 groups in FEV1 after hour1 (t=-0.091, df=98, p>0.05), after day 1(t=-0.838, df=98, p>0.05), after day 3 (t=-0.633, df=98, p>0.05) and during discharge (t=-0.833, df=98, p>0.05).

Table-01: Distribution of patients according to smoking status.

Smoking status	Solution 1(N=50) n (%)	Solution 2 (N=50) n (%)
Non-smoker	0(0)	1(2)
Present smoker	31(62)	22(44)
Ex-smoker	19(38)	27(54)

In solution-1 group most patient (31, 62%) were present smoker and in solution-2 group most patient (27, 54%) were ex-smoker. There was 1 non-smoker in solution-2 group.

Table-02: Distribution of patients according to disease duration.

Duration of	Solution 1(N=50)	Mean	Solution 2(N=50)	Mean

disease(years)	n (%)	(±SD)	n (%)	(±SD)
<5	3(6)		3(6)	
5-10	34(68)	7.60	39(78)	7.24
>10	13(26)	(±1.84)	8(16)	(±2.02)

The mean duration of disease in solution-1 and solution-2 were 7.60 (±1.84) and 7.24(±2.02) respectively.

Table-03: Distribution of patients according to hospital stay.

Hospital stay	Solution 1(N=50) Mean (±SD)	Solution 2(N=50) Mean (±SD)	t (p)
	5.98 (±1.67)	5.8 (±1.39)	0.586 (>0.05)

The mean hospital stay in solution-1 and solution-2 groups were 5.98(±1.67) and 5.8(±1.39) respectively. No difference was observed in the hospital stay between the two groups (t=0.586, (p>0.05).

DISCUSSION

The present study evaluated the effect of combined nebulized salbutamol and ipratropium bromide on spirometric parameters in patients with acute exacerbation of COPD. The mean age of patients in the salbutamol group and combination therapy group were 58.9(±7.68) years and 57.78(±8.06) years respectively, with the majority being above 60 years of age. Similar age distribution was observed in previous studies conducted by Moayyedi *et al.,* [17] and Friedman *et al.,* [18], although their patients were relatively older. Earlier presentation of COPD in our study population may be associated with smoking, occupational dust exposure, undernutrition, and lower socioeconomic conditions.

The predominance of male patients in our study is consistent with the smoking pattern in Bangladesh, where smoking prevalence remains considerably higher among men. Friedman *et al.,* [18] reported a greater proportion of female COPD patients compared with our findings.

Spirometric assessment revealed improvement in pulmonary function parameters following bronchodilator therapy in both groups. Mean FEV1 and FVC values improved progressively during hospitalization. However, the addition of ipratropium bromide to salbutamol did not produce statistically significant additional improvement in spirometric indices compared with salbutamol alone. Similar observations were reported by several previous investigators [19-20].

Some earlier studies demonstrated greater bronchodilator response with combination therapy in terms of airway obstruction and spirometric improvement [21-23]. Differences in study design, patient selection, disease severity, duration of follow-up, and baseline lung function may explain these variations. Many of those studies were conducted among stable COPD patients, whereas our study focused specifically on acute exacerbation.

No significant difference in hospital stay was observed between the two groups in our study, which is comparable to findings reported by Friedman *et al.,* [18] and Moayyedi *et al.,* [17]. Our results therefore suggest that combination therapy does not significantly influence short-term clinical outcome or duration of hospitalization in acute exacerbation of COPD.

O'Driscoll *et al.,* [14] demonstrated that combination therapy provided no additional benefit during the initial hour of treatment in acute exacerbation of COPD. Similarly, Easton *et al.,*[20] found no significant difference between salbutamol and ipratropium bromide regarding bronchodilator efficacy. Our findings are consistent with these observations.

In the present study, spirometric parameters including FEV1 and FVC were used as objective markers of bronchodilator response because they are more reliable than serial peak flow measurements. However, it is well recognized that spirometric improvement may not always correlate with subjective sensation of dyspnea and exercise tolerance [24-27]. Therefore, clinical assessment remains important during management of COPD exacerbation.

Although combined nebulized salbutamol and ipratropium bromide showed some degree of spirometric improvement, the additional benefit over salbutamol alone was not statistically significant in our study. Considering the increased treatment cost and possibility of anticholinergic adverse effects, routine use of combination therapy in all hospitalized patients with acute exacerbation of COPD may not be justified. Nevertheless, combination therapy may still be useful in selected patients with inadequate response to β2 agonist therapy alone.

CONCLUSION

Both nebulized salbutamol alone and its combination with ipratropium bromide improved spirometric parameters in acute exacerbation of COPD. The combination showed a slight additional

improvement in FEV1 and FVC, but this was not statistically significant. No significant difference was found between the two groups in symptom relief or hospital stay duration. Given the higher cost and potential anticholinergic side effects, routine use of combination therapy may not be justified. However, it may be considered in patients with inadequate response to salbutamol alone.

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