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Effectiveness Of Glycopyrronium Plus Indacaterol Combination in Patients with Moderate to Severe Chronic Obstructive Pulmonary Disease

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ABSTRACT

Background: Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of morbidity and mortality worldwide, particularly in low- and middle-income countries. Dual bronchodilator therapy using long-acting β_2-agonists (LABA) and long-acting muscarinic antagonists (LAMA) is recommended for moderate to severe COPD in improving lung function and symptom control.
Methods: This randomized prospective interventional study was conducted at a tertiary care center in North India from July 2024 to December 2025.A total of 104 patients with moderate to severe COPD diagnosed by GOLD criteria were included and randomized.All patients received inhaled Glycopyrronium/Indacaterol (50/110 µg) once daily for 12 weeks.Spirometry was performed at baseline, 6 weeks, and 12 weeks.Effectiveness was assessed by changes in forced expiratory volume in one second (FEV_1), while tolerability was evaluated by recording adverse events.Statistical analysis was conducted using SPSS 26.0, with $p < 0.05$ considered significant.
Results: Mean FEV_1 improved significantly from 60.70 + 12.47 predicted at baseline to 61.83+11.36 at 6 weeks and 69.65+11.66 at 12 weeks. ($p = 0.001$). The treatment was well tolerated with mild adverse events such as dry mouth,throat irritation and cough.
Conclusion: Glycopyrronium/Indacaterol demonstrated significantly improved lung function and well tolerated over 12 weeks, suggesting it its effectiveness and safety in long-term management of moderate to severe COPD.

Keywords*: Chronic Obstructive Pulmonary Disease, bronchodilator therapy, Mean FEV, Glycopyrronium .*

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a major global health concern and ranks among the leading causes of mortality worldwide, with a disproportionately high burden in low and middle-income countries. It is a heterogeneous respiratory disorder characterized by persistent respiratory symptoms such as dyspnea, cough, sputum production, and recurrent exacerbations due to airway inflammation and progressive airflow limitation.[1]

The pathogenesis of COPD involves complex interactions between genetic susceptibility and environmental exposures throughout life. Cigarette smoking remains the most significant risk factor, contributing to accelerated decline in lung function and increased mortality. Passive smoking and prenatal exposure further increase susceptibility. In developing countries like India, non-smoking risk factors such as biomass fuel exposure, occupational hazards, and air pollution play a substantial role.[2-4] Genetic factors, particularly α-1 antitrypsin deficiency, along with advancing age, prior pulmonary infections, asthma and low socioeconomic status also contribute to disease development.[5]

COPD is associated with chronic inflammation, airway remodeling, and destruction of lung parenchyma, particularly affecting small airways. Structural changes such as mucus hypersecretion, fibrosis, and loss of elastic recoil lead to progressive airflow limitation.[6-7] Exacerbations are a hallmark feature of COPD and significantly impact disease progression, healthcare utilization and mortality.[8]
Diagnosis of COPD is primarily based on spirometry, with a post-bronchodilator FEV_1/FVC ratio of less than 0.7 confirming persistent airflow limitation.[9] Disease assessment also includes symptom evaluation using tools such as the COPD Assessment Test (CAT) and modified Medical Research Council (mMRC) dyspnea scale.[10]

Globally, COPD affects over 400 million individuals and is a major contributor to healthcare burden, with rising prevalence due to aging populations, tobacco use and environmental pollution.[11,12,13] Preventive strategies focus on reducing exposure to risk factors including smoking cessation, improved ventilation and cleaner fuel use. Smoking cessation remains the most effective intervention to slow disease progression.

Management includes both non-pharmacological and pharmacological approaches. Long-acting bronchodilators, including long-acting β_2-agonists (LABA) and long-acting muscarinic antagonists (LAMA) form the cornerstone of therapy. Combination LABA/LAMA therapy has been shown to improve lung function, reduce symptoms, and decrease exacerbations more effectively than monotherapy.[14-19]

METHODS

The present study was designed as an interventional study involving patients diagnosed with Chronic Obstructive Pulmonary Disease (COPD). Study participants included COPD patients presenting to both the outpatient and inpatient departments of the Department of Tuberculosis and Respiratory Diseases at Sri Guru Ram Das Institute of Medical Sciences and Research, Vallah, Amritsar.

Inclusion Criteria:
Both outpatients and inpatients diagnosed with COPD according to GOLD criteria based on spirometry were included in the study. COPD was suspected in patients presenting with chronic cough, dyspnea, and sputum production, with or without a history of exposure to risk factors. The diagnosis was confirmed using spirometry in this clinical setting. A post-bronchodilator FEV_1/FVC ratio of <0.70 established the presence of persistent airflow limitation, confirming COPD in patients with relevant symptoms and significant exposure to noxious agents.

Exclusion Criteria:
1. Pregnant and/or nursing mothers
2. Patients with history of asthma
3. Known underlying cardiovascular abnormalities (arrhythmias, congestive heart failure, coronary artery disease)
4. Patients with history of hospitalization for pneumonia within 3 months of enrolment.
5. Patients with history of use of oral/parenteral corticosteroid or depot corticosteroid use 6 weeks and 3 months before the enrolment.
6. Contraindications/hypersensitivity to any of the study drugs.

Sampling Procedure: Open label, non blinded
Patients meeting inclusion and exclusion criteria –
1) Patients who were already diagnosed and taking medication for COPD at the time of the screening visit discontinued their previous treatment for 2 weeks and were switched to rescue medication with salbutamol DPI as monotherapy.
2) Newly diagnosed cases of COPD directly joined randomization at the time of the screening visit.

Sample Size: COPD patients presenting to the outpatient and inpatient departments of TB and Respiratory Diseases during the period from July 2024 to December 2025 at Sri Guru Ram Das Institute of Medical Sciences and Research, Vallah, Amritsar, were included in the study.

Data Collection: The purpose of the study was explained to all patients, and written informed consent was obtained prior to enrollment. All eligible cases were subjected to detailed history taking regarding symptomatology and risk factors of asthma as per a pre-designed proforma. Demographic parameters including age, sex, weight, and height were recorded. A thorough general physical examination and systemic examination were conducted, with special emphasis on the respiratory system. Routine investigations including complete blood count (CBC), fasting blood sugar (FBS), and chest radiograph were performed in all patients.

All enrolled patients received Glycopyrronium/Indacaterol dry powder inhaler (50/110) administrated once daily for 12 weeks.Spirometry was performed at baseline (day 1),6 weeks (day 42) and 12 weeks (day 84).The primary outcome measure was change in FEV1 over the study period.Patients were monitored throughout follow up for treatment adherence and adverse drug reactions to assess tolerability.

Statistical analysis

Data were analyzed using SPSS v26.0. Continuous variables were expressesd as mean ± standard deviation, whereas categorical variables were presented as frequencies and percentages. Repeated measures ANOVA was used to compare spirometric parameters over time.A p-value <0.05 was considered statistically significant.

RESULTS

DEMOGRAPHIC DATA

TABLE 1: SHOWING AGE AND SEX DISTRIBUTION OF COPD PATIENTS

Among 104 participants, 43 were females and 61 were males, demonstrating male predominance. The majority of patients belonged to 51-60 years age group.

Age Group (Yrs.)					
	Females		Males		
	No. of Patients	%age	No. of Patients	%age	Total
< 20					
21-30	0	0.0	1	1.6	1
31-40	3	7.0	7	11.5	10
41-50	15	34.9	9	14.8	24
51-60	11	25.6	26	42.6	37
61-70	12	27.9	10	16.4	22
> 70	2	4.7	8	13.1	10
Total	43	100	61	100	104

CLINICAL PRESENTATION

TABLE 2: SHOWING FREQUENCY OF SYMPTOMS AMONG COPD PATIENTS

Symptoms	No. of cases	Percentage
Cough	85	81.7
Shortness of breath (SOB)	16	15.4
Expectoration	73	70.2

Cough was the most predominant symptom, reported by 85(81.7%) patients, followed by expectoration in 73(70.2%) patients and shortness of breath in 16(15.4%) patients.

RISK FACTORS

TABLE 3: SHOWING FREQUENCY OF RISK FACTORS AMONG COPD PATIENTS

Risk factors	No. of cases	Percentage
Biomass fuel exposure	24	23.1
Smoking	15	14.4
Past H/O PTB	5	4.8

Exposure to biomass fuel exposure was most common risk factor, identified in 24 (23.1%) patients. Smoking was reported by 15 (14.4%) patients whereas past history of TB was present in 5 (4.8%) patients.

CHANGE IN PULMONARY FUNCTION

TABLE 4 : ASSOCIATION OF FEV1 VALUES ON FOLLOW UP PERIOD

	Mean	SD	f-value	p-value
FEV1 Baseline	60.70	12.47		
FEV1 at 6weeks	61.83	11.36		
FEV1 at 12 weeks	69.65	11.66	8.726	0.001

The mean FEV1 showed a progressive improvement during the 12 week treatment with Glycopyrronium /Indacaterol.The baseline mean FEV1 was 60,79+12.47, which increased to 61.83+11.36 at 6 weeks and further improved to 69.65+11.66 at 12 weeks.

Repeated ANOVA demonstrated improvement in FEV1 over time was statistically significant (f=8.726,p=0.001), indicating that treatment with Glycopyrronium/Indacaterol combination was associated with significant improvement in lung function.

DISCUSSION

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of morbidity and mortality worldwide and continues to impose a significant burden, particularly in low- and middle-income countries. The prevalence is expected to rise due to increasing exposure to risk factors and aging populations. Spirometry remains the cornerstone for diagnosis, prognostication, and monitoring treatment response, with forced expiratory volume in one second (FEV_1) serving as a key indicator of airflow limitation.

In the present study, 104 patients were analyzed, comparable in baseline characteristics including age and sex, indicating appropriate randomization. The majority of patients belonged to the 51–70 years age group, reflecting the increased prevalence of COPD in older populations, consistent with previous studies and global reports[20]. A slight male predominance was observed, which aligns with findings from other clinical studies. However, a considerable proportion of females were also affected, likely due to biomass fuel exposure, a major risk factor in developing countries.

The magnitude of improvement observed in the present study highlights the advantage of combining two long-acting bronchodilators with complementary mechanisms of action. These findings are in concordance with previous large-scale trials and subgroup analyses, including those by Gon et al.[21] and Martinez et al.[22], which reported significant improvements in trough FEV_1 with GF compared to placebo as well as mono-component therapies.

Similarly, treatment with glycopyrronium/indacaterol (GI) in the present study resulted in statistically significant improvements in FEV_1 at both 6 weeks ($p = 0.001$) and 12 weeks ($p = 0.001$), with a progressive increase in lung function over the study duration. This gradual and sustained response reflects the additive bronchodilatory effect of combining a LAMA with a LABA. These results are consistent with earlier clinical studies, including those by Vincken W, et al.[23] and Salomon J, et al.[24], which demonstrated that combination therapy with glycopyrronium and indacaterol provides superior improvement in lung function parameters compared to indacaterol monotherapy.

The primary outcome demonstrated that both treatment groups showed progressive improvement in FEV_1 over time. At baseline and 6 weeks, no statistically significant difference was observed between the groups. However, at 12 weeks, Glycopyrronium/Indacaterol showed significantly greater improvement in FEV_1 indicating superior long-term bronchodilation with Glycopyrronium/Indacaterol. These findings are supported by previous studies demonstrating sustained bronchodilation and improved clinical outcomes with Indacaterol-based therapy.[25]

The enhanced efficacy of the GI combination may be attributed to the pharmacological properties of Indacaterol, an ultra-long-acting β_2-agonist providing sustained 24-hour bronchodilation as compared to Formoterol.

Although this study adds to the growing body of evidence supporting dual bronchodilator therapy in COPD management, glycopyrronium/indacaterol combination demonstrated comparable and clinically significant improvements in lung function. However, glycopyrronium/indacaterol demonstrated superior improvement in FEV_1 and symptom control at 12 weeks, suggesting its advantage in long-term management of moderate to severe COPD. However, the study has several limitations, including a relatively small sample size and short follow-up duration, which may limit generalizability and the assessment of long-term outcomes. The single-center design and lack of blinding may also introduce bias. Future studies should include larger, multicenter populations with longer follow-up, incorporate blinding, and evaluate exacerbation rates, quality of life, and long-term safety to better guide clinical practice.

CONCLUSION

In conclusion, the present study demonstrated that Glycopyrronium/Indacaterol has significant improvement in FEV_1 and symptom control at 12 weeks, suggesting its advantage in long-term management of moderate to severe COPD.

LIMITATIONS

The study was conducted at a single center with a relatively short follow-up period of 12 weeks. Patient-reported outcomes such as CAT score,mMRC dyspnea score, quality of life, exercise capacity, and exacerbation rates were not analyzed during follow-up . Larger multicenter studies with longer follow-up are required to evaluate the long-term effectiveness, safety, exacerbation prevention, and quality-of-life benefits of Glycopyrronium/Indacaterol therapy.

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