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Indacaterol/ Glycopyrronium in Symptomatic Patients with COPD (GOLD 2 and GOLD 3) Versus Salmeterol/ Fluticasone

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ABSTRACT

Background: Chronic Obstructive Pulmonary Disease (COPD) is a significant global health concern with increasing prevalence and substantial economic and social impacts. It is a leading cause of mortality, affecting millions worldwide. COPD severity is classified using the Global Initiative for Chronic Obstructive Lung Disease (GOLD) system, categorizing patients based on symptoms, airflow limitation, and exacerbation history. Treatment primarily involves long-acting bronchodilators, including LABAs and LAMAs. Indacaterol/glycopyrronium (IND/GLY) and salmeterol/fluticasone (SFC/FLU) are widely used therapies, however, direct comparisons remain limited. This study aims to compare IND/GLY and SFC/FLU in symptomatic COPD patients, evaluating their impact on symptom improvement using CAT scores. **Methods:** This was a randomized controlled trial conducted at Pulmonology Department, Allied-2 Hospital Faisalabad from 15 July 2024 to 15 January 2025. A total number of 266 patients were allocated to each treatment group. Outcomes were noted in terms of changes in the CAT score and the occurrence of adverse effects. **Results:** Of the 266 patients, 184 (69.2%) were male and 82 (30.8%) were female patients. Mean age of the patients was 48.16±6.81 years. Eighty-four (63.2%) patients had severe COPD. There was no significant difference in group-wise distribution of patients in both groups (p-0.265). Mean pretreatment CAT score was 28.49±4.311 in IND/GLY group and 28.86 ± 4.291 in SAL/FLU group. The post-treatment CAT score was 16.52 ± 3.378 in IND/GLY group and 16.97 ± 4.59 in SAL/FLU group. **Conclusion:** Salmeterol-fluticasone and indacaterol-glycopyrronium both improved lung function metrics and the quality of life in people with COPD while having little side effects. There was no significant difference in safety or effectiveness.

INTRODUCTION

COPD is a disease that has major health-care, economic, and social impacts[1]. Over the last several decades, a growing trend in COPD prevalence has been seen, and is expected to continue increasing[2]. COPD is presently the fourth biggest cause of mortality globally, with 251 million cases reported. In Asia, the estimated COPD prevalence was 6.2%, with 19.1% of individuals having severe COPD[3].

Using the Global Initiative for Chronic Obstructive Lung Disease (GOLD) approach, patients with COPD are categorized into GOLD groups A through D according to their own risk factors, including symptoms, history of exacerbations, and airflow limitation. GOLD B patients have high symptom burden and mild (GOLD I) or moderate (GOLD II) lung function impairment with a lower risk of exacerbation, while GOLD D patients have high symptom burden and severe (GOLD III) lung function impairment and/or a history of exacerbations[4].

The cornerstone of pharmacological treatment for COPD is inhaled long-acting bronchodilators, or LABDs. Health-related quality of life and lung function are enhanced by LABDs, such as long-acting muscarinic antagonists (LAMAs) and long-acting β2-agonists (LABAs). A mainstay in the treatment of COPD is salmeterol-fluticasone (SFC), a combination of corticosteroids and long-acting beta-agonists. For the maintenance therapy of COPD, the dual bronchodilator indacaterol/glycopyrronium (IND/GLY), which combines LABA (indacaterol) and LAMA (glycopyrronium), is approved. Patients with a history of infrequent exacerbations who continue to experience symptoms while using long-acting monotherapy are recommended to take IND/GLY[5]. Few trials have compared the effectiveness of IND/GLY and SFC/FLU in treating COPD, despite the fact that both therapeutic approaches are widely used. The majority of the material currently in publication concentrates on individual assessments of either pharmaceutical regimen, therefore a direct comparison is required in order to effectively

assist doctors[6]. A study on comparing two treatments regimes reported pre-treatment CAT score of 24 ± 3.9 in group A (IND/GLY) and 23 ± 3.2 in group B(SFC). The CAT score also improved significantly in both groups (16 ± 2.8 versus17 ±3.0)[7].

The aim of this study was to compare Indacaterol/glycopyrronium in symptomatic patients with COPD and salmeterol/fluticasone in terms of mean decrease in CAT score. This study provides insights into optimizing COPD management strategies in a tertiary care hospital of Faisalabad. The drug combination with better results will be recommended in future.

MATERIAL AND METHODS

Study Design, Setting, and Duration

This randomized controlled trial was conducted in the Department of Pulmonology, Allied Hospital-2, Faisalabad in six months from July 15, 2024 to January 15, 2025.

Sample Size

The sample size was calculated using the OpenEpi calculator for two means, with a 5% level of significance and 80% power of the test The anticipated mean CAT score in Group A was 16 ± 2.8[6] and in Group B was 17 ±3.0[7]. The final sample size was 266 patients.

Sampling Technique

Non-probability, consecutive sampling technique was used.

Sample Selection

Inclusion Criteria

- Both genders
- Age >40 to 60 years
- Confirmed Diagnosis of COPD according to GOLD criteria
- Patients with GOLD 2 and Gold 3

Exclusion Criteria

- Co-morbid Condition such as other respiratory disorders, including asthma, lung cancer, and interstitial lung disease
- Use of any medication that could interact with the study drugs
- Any cognitive impairment or psychiatric condition

Methodology

The study was started after the approval of the study from Institutional ethical review committee and CPSP. Informed consent was taken from each participant (before inclusion) to participate in this study. CAT score was calculated at baseline. Patients were selected according to inclusion criteria and divided into two groups. Group A was given Indacaterol-Glycopyrronium110/50 µg once daily (o.d.) and group B was given Salmeterol-Fluticasone): 50/250 µg twice daily (b.i.d.) for 12 weeks. Spirometry was performed using the Spirolab 3 model spirometer. CAT score was calculated after 12 weeks. All the collected information data was entered into SPSS version 25. Mean and standard deviation was calculated for all quantitative variable like age, weight, height, BMI, duration of COPD and CATS score. Frequency and percentage were calculated for all qualitative variables like gender, smoking status and severity of COPD (GOLD2/3). Independent sample t-test was applied to compare CAT score in both groups. A p-value less than or equal to 0.05 was considered statistically significant.

RESULTS

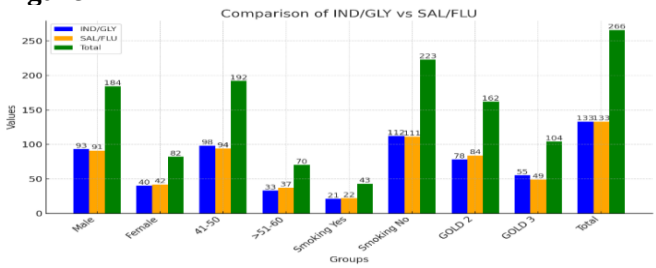
Of the 266 patients, 184 (69.2%) were male and 82 (30.8%) were female. There was no significant difference in group-wise distribution of patients in both groups (p-0.447). There were 93(69.9%) males in group A and 91(68.4) in group B. While there were 40(30.1%) females in group A and 42(31.6%) females in group B. Mean age of the patients was 48.16±6.81 years, minimum age was 40 and maximum age was 60 years. Of the 266 patients, 192 (73.3%) were aged 41-50 years and 70 (26.7%) were aged 51-60 years. There was no significant difference in group wise distribution of patients in both groups (p 0.338%). There were 43(16.2%) smokers and 223(83.8%) were non-smokers. There was no significant difference in group wise distribution of patients in both groups (p 0.500). Regarding the severity of COPD, 78 (58.6%) patients had moderate COPD and 84 (63.2%) had severe COPD. There was no significant difference in group wise distribution of patients in both groups (p 0.265%).

Table 1

Basic Demographic Characters of Patients

Variables		Group		Total	P=Value
		IND/GLY	SAL/FLU		
Gender	Male	93(69.9)	91(68.4)	184(69.2)	
	Female	40(30.1)	42(31.6)	82(30.8)	0.447
Age Group	41-50	98(74.8)	94(71.8)	192(73.3)	
	>51-60	33(25.2)	37(28.2)	70(26.7)	0.338
Smoking	Yes	21(15.8)	22(16.5)	43(16.2)	
	No	112(84.2)	111(83.5)	223(83.8)	0.500
COPD Severity	GOLD 2	78(58.6)	84(63.2)	162(60.9)	
	GOLD 3	55(41.4)	49(36.8)	104(39.1)	0.265
Total		133(100)	133(100)	266(100)	

Figure 1



The mean pre-treatment CAT score was 28.49 ± 4.311 in IND/GLY group and 28.86 ± 4.291 in SAL/FLU group.

The post-treatment CAT score was 16.52 ± 3.378 in IND/GLY group and 16.97 ± 4.59 in SAL/FLU group. There was no significant difference in post-treatment CAT score (p 0.382) which shows that both the drug combination is effective to treat COPD.

Table 2

Pre and Post-Treatment CAT Score

CAT Score	Group	Mean	Std. D	P=Value
Pre-treatment	IND/GLY	28.49	4.311	.485
	SAL/FLU	28.86	4.291	
Post-treatment	IND/GLY	16.52	3.78	.382
	SAL/FLU	16.97	4.592	

Side effects were low in both groups, with no significant difference between them

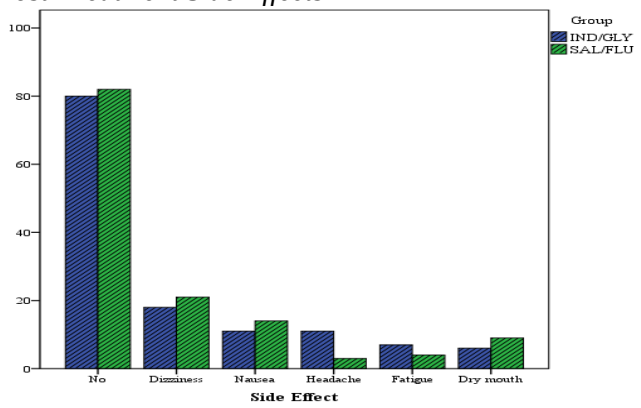
Table 3

Side Effects in Both Groups

Side Effect	Group		P=Value
	IND/GLY	SAL/FLU	
No	80(60.2)	82(61.7)	0.252
Dizziness	18(13.5)	21(15.8)	
Nausea	11(8.3)	14(10.5)	
Headache	11(8.3)	3(2.3)	
Fatigue	7(5.3)	4(3.0)	
Dry mouth	6(4.5)	9(6.8)	
Total	133(100.0)	133(100.0)	

Figure 2

Post-Treatment Side Effects



DISCUSSION

COPD is a condition that has a big influence on society and healthcare[8]. According to the GOLD Study, COPD accounts for around one-fifth of all deaths globally as well as years lost due to early morbidity and impairment[1]. Based on the severity of COPD, the evaluation of symptoms, and the history of exacerbations, the GOLD approach suggests COPD maintenance treatment[9, 10]. Although ICS constitute the cornerstone of asthma therapy, their applicability to COPD is up for discussion. When used in conjunction with dual bronchodilator medication (triple therapy), ICS significantly reduced (~25%) the frequency of exacerbations in patients with COPD who experienced frequent or severe exacerbations, according to recent RCTs[9, 11].

The aim of this study was to compare Indacaterol/glycopyrronium in symptomatic patients with COPD and salmeterol/fluticasone in terms of mean decrease in CAT score. From total 266 patients, there were 184(69.2) males and 82(30.8) female patients. Mean age of the patients was 48.16±6.81 years, minimum age was 40 and maximum age was 60 years. There were 43(16.2) smokers and 223(83.8) were non-smokers. There were 78 (58.6%) patients with moderate COPD and 84 (63.2%) with severe COPD. There was no significant difference in group wise distribution of patients in both groups (p 0.265)). These characteristics are consistent with findings from other studies[2, 7, 12].

The post-treatment CAT score was 16.52 ± 3.378 in the IND/GLY group and 16.97 ± 4.59 in the SAL/FLU group. There was no significant difference in post-treatment CAT score (p 0.382) indicating that both drug combinations were effective in treating COPD. Our analysis also revealed a considerable reduction in CAT scores in both groups post-treatment. This is in line with other research showing that long-acting bronchodilators improve the quality of life for people with COPD[13]. These results are consistent with other studies showing that long-acting bronchodilators are useful for controlling symptoms and preventing flare-ups of COPD[3, 14].

Both drugs had well-tolerated safety profiles with little side effects, which is consistent with other studies that support the safety of these pharmacological classes[15]. In both groups, the incidence of dry mouth, lightheadedness, and nausea was low and similar.

In the Singaporean healthcare system, IND/GLY was shown to be more cost-effective than SFC for patients with moderate-to-severe COPD who are at low risk of exacerbations. The study concludes that, in the Singaporean healthcare system, IND/GLY was shown to be significantly more cost-effective than SFC for patients with moderate-to-severe COPD who are not at high risk of exacerbations[4, 5, 16].

CONCLUSION

Both salmeterol-fluticasone and indacaterol-glycopyrronium improved lung function metrics and the quality of life in COPD patients, with minimal side effects. There was no significant difference in safety or effectiveness between the two treatments.

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