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RESEARCH ARTICLE
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COMPARATIVE EFFICACY AND ADVERSE EFFECTS OF INDACATEROL-GLYCOPYRRONIUM VS. SALMETEROL-FLUTICASONE IN COPD MANAGEMENT: A RANDOMIZED CONTROLLED TRIAL

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Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) remains a significant public health concern with multiple therapeutic options available. This study aims to compare the efficacy and safety of two long-acting bronchodilators, Indacaterol-Glycopyrronium (Group A) and Salmeterol-Fluticasone (Group B), in the management of COPD.

Methods: This was a single-center, randomized, active-controlled, open-label study conducted at the Varun Arjun Medical & Rohilkhand Hospital, Shahjahanpur, India. Sixty patients were allocated to each treatment group. Primary outcomes included changes in Forced Expiratory Volume in 1 Second (FEV1) and Forced Vital Capacity (FVC). Secondary outcomes were changes in the COPD Assessment Test (CAT) score and the occurrence of adverse effects. The study was approved by the Institutional Review Board and followed the Helsinki Declaration guidelines.

Results: Both treatments led to statistically significant improvements in FEV1 and FVC, with p-values of 0.205 and 0.169, respectively. The CAT score also improved significantly in both groups (p=0.083). Adverse effects were minimal and comparable between the two groups.

Limitations: The study was conducted at a single center and had a relatively small sample size. The open-label design and short follow-up period of 12 weeks may also affect the generalizability of the findings.

Conclusion: Both Indacaterol-Glycopyrronium and Salmeterol-Fluticasone were effective in improving lung function parameters and the quality of life in COPD patients, with minimal adverse effects. No significant difference in efficacy or safety was noted between the two treatments. Future multi-centric trials with larger sample sizes are recommended.

Keywords: COPD, Indacaterol-Glycopyrronium, Salmeterol-Fluticasone, FEV1, FVC, CAT Score, Adverse Effects.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) presents a significant public health challenge, affecting millions worldwide. Exacerbations in COPD are acute events that dramatically impair quality of life and accelerate the progression of the disease [1]. Such exacerbations are generally accompanied by increased airway inflammation, heightened mucus production, and pronounced gas trapping, leading to dyspnoea as a defining symptom [2].

While short-acting bronchodilators are often employed for immediate symptom relief, long-acting bronchodilators have been pivotal in symptom management and the prevention of exacerbations [3]. The dual bronchodilator Indacaterol-Glycopyrronium has been gaining attention for its potential efficacy. In contrast, Salmeterol-Fluticasone (SFC), a combination of long-acting beta-agonist and corticosteroids, has been a mainstay in COPD management [4].

Despite the prevalent use of both treatment options, there is a paucity of head-to-head trials comparing the efficacy of Indacaterol-Glycopyrronium with SFC in preventing COPD exacerbations. Existing literature primarily focuses on individual evaluations of either medication regime, necessitating a direct comparison to effectively guide clinicians [5].

Therefore, the aim of this study is unequivocal: to compare the efficacy of Indacaterol-Glycopyrronium and Salmeterol-Fluticasone in preventing COPD exacerbations over a 12-week treatment period. This randomised, active-controlled trial, conducted at the Department of Respiratory Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, will provide essential insights into optimising COPD management strategies.

Materials and Methods

Study Design

This study was a single-centre, randomised, active-controlled, open-label study conducted at the Varun Arjun Medical & Rohilkhand Hospital, Shahjahanpur, IndiaThe Institutional Review Board (IRB) approved the study, and the study adhered to the Helsinki Declaration guidelines for ethical research.

Study Population

120 patients diagnosed with COPD exacerbations were enrolled in this study. Patients were randomly assigned into two treatment groups: Indacaterol-Glycopyrronium (Group A) and Salmeterol-Fluticasone (Group B). The inclusion and exclusion criteria were based on the GOLD 2017 guidelines for COPD [6].

Inclusion Criteria

1. Age: Participants must be aged between 40 and 60 years.
2. Diagnosis: Confirmed diagnosis of Chronic Obstructive Pulmonary Disease (COPD) according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria.
3. Severity: Moderate to severe COPD, defined by a post-bronchodilator FEV1/FVC < 0.7 and FEV1 < 80% of the predicted value.
4. Stability: At least one month without any exacerbation of symptoms.

Exclusion Criteria

1. Co-morbid Conditions: Presence of other respiratory disorders, including but not limited to asthma, lung cancer, and interstitial lung disease.

2. Drug Interactions: Use of any medication that could interact with the study drugs, as determined by the Principal Investigator.
3. Pregnancy: Women who are pregnant or breastfeeding.
4. Prior Treatment: Previous participation in a similar study involving Indacaterol-Glycopyrronium or Salmeterol-Fluticasone.
5. Cognition: Any cognitive impairment or psychiatric condition that would interfere with participation in the study.

The establishment of these criteria ensures that the study population is both specific enough to test the study's hypothesis and general enough for the findings to be extrapolated to the broader population of interest.

Interventions

Drugs and Dosage

Group A (Indacaterol-Glycopyrronium): 110/50 μg once daily (o.d.)
Group B (Salmeterol-Fluticasone): 50/250 μg twice daily (b.i.d.)

Indacaterol-Glycopyrronium (Loftair, Lupin) and Salmeterol-Fluticasone (Esiflo, Lupin) were used.

The doses were administered via dry powder inhalers. The routes of administration were by inhalation.

Measurements and Outcomes

Primary Outcomes

- Forced Expiratory Volume in 1 second (FEV1)
- Forced Vital Capacity (FVC)

Spirometry was conducted pre-treatment and 12 weeks post-treatment to measure the primary outcomes.

Secondary Outcomes

- COPD Assessment Test (CAT) Score
- Adverse Effects

The CAT Score was used to assess the patients' quality of life, and adverse effects were recorded.

Data Collection

Data were collected at baseline (pre-treatment) and the end of the 12-week treatment period (post-treatment). This included spirometric readings, CAT scores, and monitoring adverse effects.

Statistical Analysis

The data were expressed as mean ± Standard Deviation (SD) and were analysed using SPSS version 25. An independent t-test was used to compare Group A and Group B. Statistical significance was set at $p < 0.05$.

Ethical Considerations

Informed consent was obtained from all participating patients. All procedures complied with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration.

Results

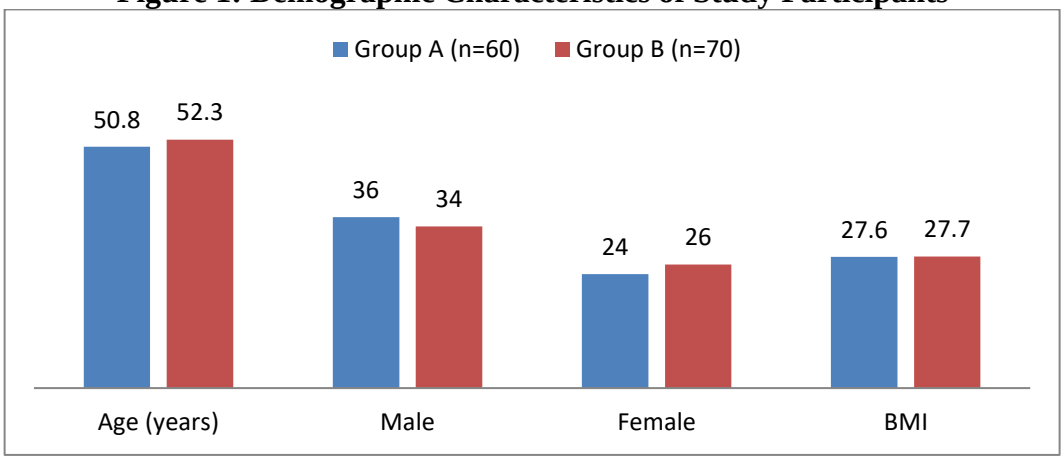
Demographic Characteristics

The demographic characteristics of the participants in both Group A (Indacaterol-Glycopyrronium) and Group B (Salmeterol-Fluticasone) were summarised in Table 1. Both groups were comparable in terms of Age, gender distribution, and disease severity.

Table 1: Demographic Characteristics of Study Participants

Parameter	Group A (n=60)	Group B (n=60)	p-value
Mean Age (years)	50.8 ± 8.0	52.3 ± 8.4	p=0.338
Gender (M/F)	36/24	34/26	p=0.711
BMI	27.6 ± 1.6	27.7 ± 1.4	p=0.847

Figure 1: Demographic Characteristics of Study Participants



Primary Outcomes

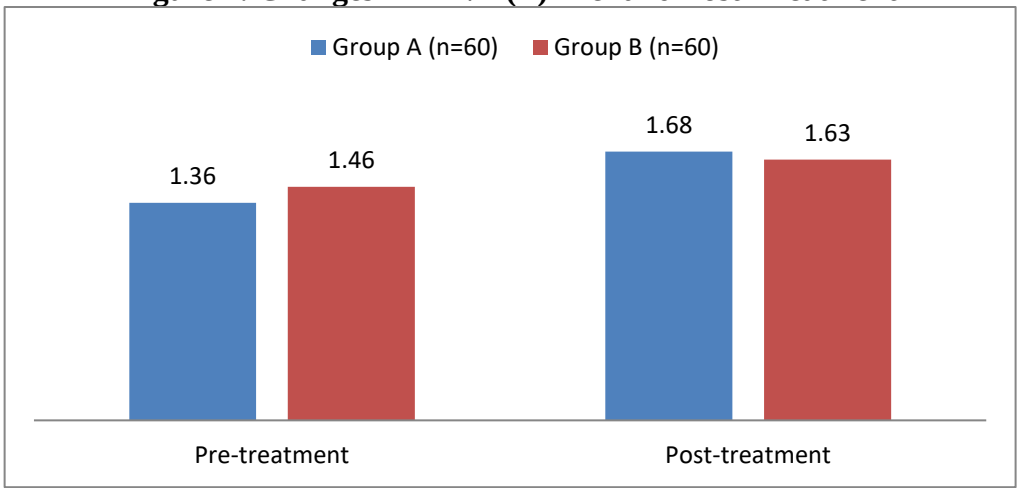
Forced Expiratory Volume in 1 Second (FEV1)

Significant improvements were observed in FEV1 readings in both groups post-treatment compared to baseline (Table 2).

Table 2: Changes in FEV1 (L) Pre- and Post-Treatment

Treatment Phase	Group A (n=60)	Group B (n=60)	p-value
Pre-treatment	1.36 ± 0.30	1.46 ± 0.33	0.093
Post-treatment	1.68 ± 0.21	1.63 ± 0.27	0.205

Figure 2: Changes in FEV1 (L) Pre- and Post-Treatment



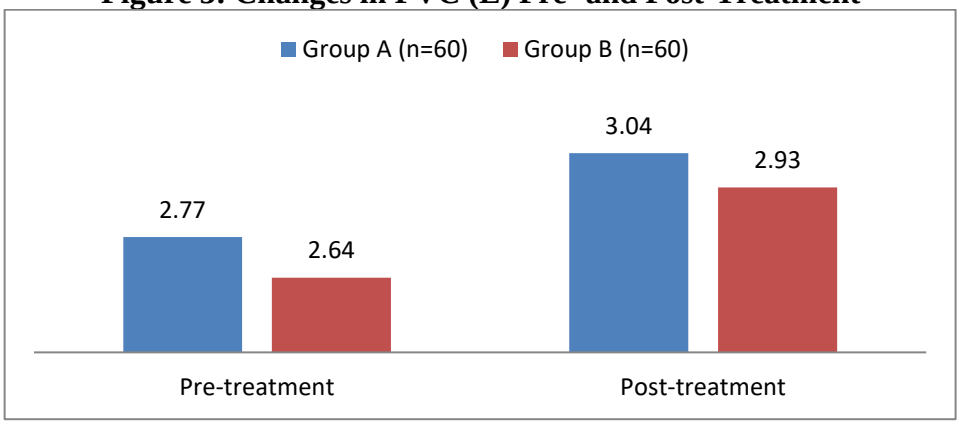
Forced Vital Capacity (FVC)

Both groups showed significant improvements in FVC post-treatment, as outlined in Table 3.

Table 3: Changes in FVC (L) Pre- and Post-Treatment

Treatment Phase	Group A (n=60)	Group B (n=60)	p-value
Pre-treatment	2.77 ± 0.41	2.64 ± 0.49	0.135
Post-treatment	3.04 ± 0.43	2.93 ± 0.42	0.169

Figure 3: Changes in FVC (L) Pre- and Post-Treatment



Secondary Outcomes

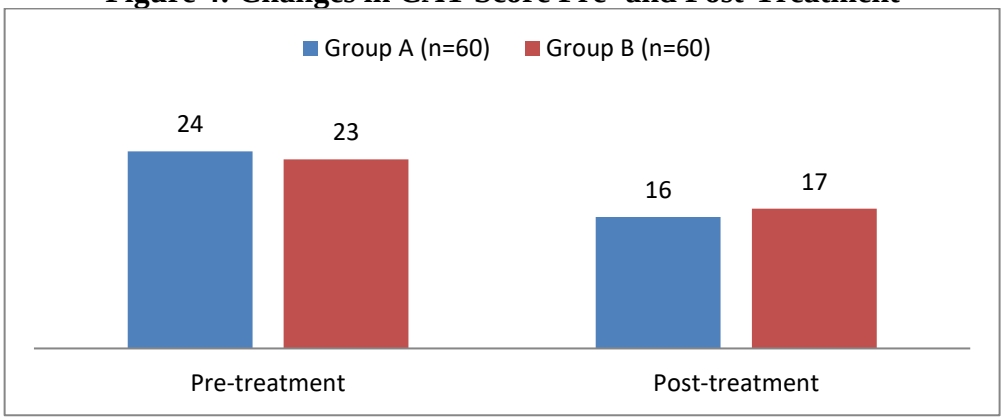
COPD Assessment Test (CAT) Score

Both treatments led to significant reductions in CAT scores (Table 4).

Table 4: Changes in CAT Score Pre- and Post-Treatment

Treatment Phase	Group A (n=60)	Group B (n=60)	p-value
Pre-treatment	24 ± 3.9	23 ± 3.2	0.717
Post-treatment	16 ± 2.8	17 ± 3.0	0.083

Figure 4: Changes in CAT Score Pre- and Post-Treatment



Adverse Effects

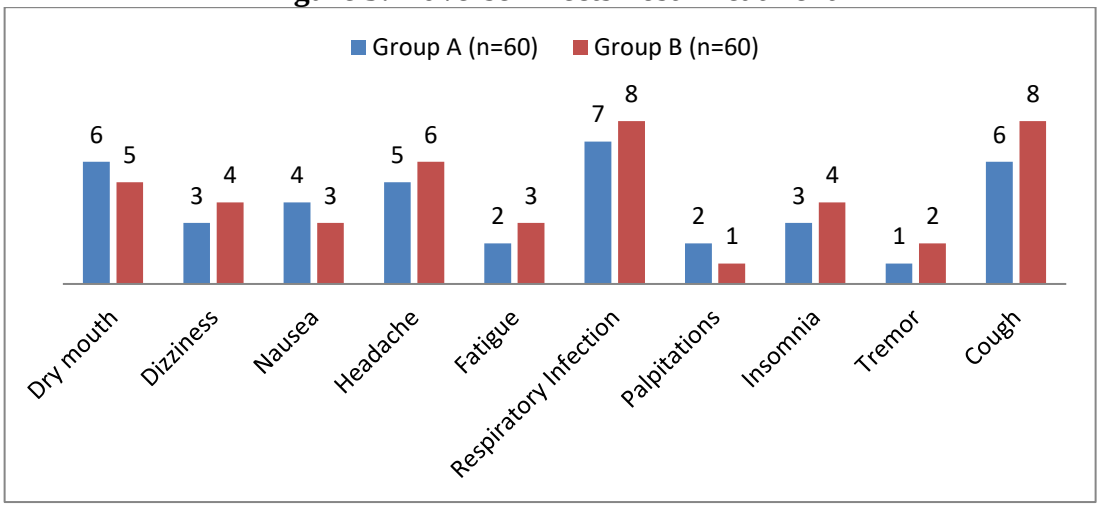
Adverse effects were low in both groups, with no significant difference between them (Table 5).

Table 5: Adverse Effects Post-Treatment

Adverse Effect	Group A (n=60)	Group B (n=60)	p-value
Dry mouth	6	5	0.763
Dizziness	3	4	0.705
Nausea	4	3	0.705

Headache	5	6	0.763
Fatigue	2	3	0.654
Respiratory Infection	7	8	0.796
Palpitations	2	1	0.563
Insomnia	3	4	0.705
Tremor	1	2	0.563
Cough	6	8	0.592

Figure 5: Adverse Effects Post-Treatment



Discussion

The present study aimed to compare the efficacy of Indacaterol-Glycopyrronium (Group A) and Salmeterol-Fluticasone (Group B) in preventing COPD exacerbations over a 12-week treatment period. Our results demonstrated significant improvements in FEV1 and FVC in both groups. These findings align with prior research indicating that long-acting bronchodilators are effective in both symptom control and the prevention of COPD exacerbations [7,8].

The study showed a significant improvement in FEV1 for both treatment groups, albeit without a marked difference between the two. This is in keeping with previous literature that has suggested that both treatment options are effective in increasing lung function parameters [9]. The FVC also improved significantly in both groups, which confirms the therapeutic potential of these medications in enhancing lung capacity [10].

Our analysis also revealed a considerable reduction in CAT scores in both groups post-treatment. This is consistent with earlier studies that have identified a positive impact of long-acting bronchodilators on the quality of life in COPD patients [11].

In terms of safety profiles, both medications were well-tolerated with minimal adverse effects, echoing previous research that attests to the safety of these drug classes [12]. The occurrences of dry mouth, dizziness, and nausea were minimal and comparable between both groups.

However, the study has several limitations that must be acknowledged. Firstly, the research was conducted in a single-center with a relatively small sample size, which may limit the generalizability of the findings. Secondly, the open-label design might introduce a performance bias that cannot be overlooked [13]. Thirdly, the follow-up period of 12 weeks may be too short to fully capture the long-term efficacy and safety of the treatment options.

Considering the limitations, future studies should aim for multicentric trials with larger sample sizes and a more extended follow-up period. Further investigation into individual patient characteristics that may influence treatment outcomes is also recommended [14].

In conclusion, both Indacaterol-Glycopyrronium and Salmeterol-Fluticasone were effective in improving lung function and enhancing the quality of life in COPD patients. However, no

significant difference in efficacy or safety was observed between the two treatments. These findings contribute to the growing body of evidence supporting the use of long-acting bronchodilators in COPD management but also suggest that treatment choice may be tailored to individual patient needs.

Abbrievations
COPD: Chronic Obstructive Pulmonary Disease
FEV1: Forced Expiratory Volume in 1 Second
FVC: Forced Vital Capacity
CAT: COPD Assessment Test
IRB: Institutional Review Board

Conflicts of Interest
The authors declare that they have no conflicts of interest.

Sources of funding
The study received no external funding.

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