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Original Research Article

Comparative Effectiveness of Dual Bronchodilator Therapy vs Triple Therapy in Moderate COPD

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Abstract: ***Background***: Moderate chronic obstructive pulmonary disease (COPD) represents a large proportion of the disease burden, and optimal maintenance therapy in this group remains controversial. Objective: To compare the clinical effectiveness of dual bronchodilator therapy versus triple therapy in patients with moderate COPD. ***Methods***: This was a comparative analytical study conducted at Imran Idrees teaching hospital Sialkot from May 2024 to May 2025 including 250 patients diagnosed with moderate chronic obstructive pulmonary disease (COPD). The study was designed to compare the clinical effectiveness of dual bronchodilator therapy versus triple therapy in terms of lung function, symptom control, exacerbation frequency, and treatment-related adverse events. ***Results***: Baseline characteristics were comparable between groups. Improvement in FEV_1 was observed in both groups, with a greater increase in the triple therapy group (5.4 ± 2.0%) compared to the dual therapy group (3.2 ± 1.5%). Annual exacerbation rates were lower with triple therapy (1.0 ± 0.5 vs. 1.4 ± 0.6), and fewer patients experienced two or more exacerbations. Symptom severity, as assessed by the CAT score, improved in both groups, with a slightly greater reduction in the triple therapy group. However, adverse events were significantly more frequent with triple therapy, including higher rates of pneumonia (11.2% vs. 3.2%), oral candidiasis (8.8% vs. 1.6%), and treatment discontinuation due to side effects. ***Conclusion***: It is concluded that while triple therapy offers modest additional benefits in lung function and exacerbation reduction in moderate COPD, it is associated with a higher risk of adverse events.

Keywords Chronic obstructive pulmonary disease, dual bronchodilator therapy, triple therapy, FEV_1, exacerbations.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) represents a progressive respiratory disease, which is manifested by airflow obstruction, chronic airway

inflammation, and acute exacerbation, which severely affects the quality of life and survival [1]. It is one of the significant health burdens worldwide as it is one of the main causes of morbidity and mortality in the globe with prevalence steadily increasing owing to the consecutive tobacco exposure, biomass fuel consumption, and growing age of the population [2]. The moderate patients with COPD generate a significant percentage of the disease spectrum and present a significant use of healthcare because of the symptom burden and frequent exacerbations [3]. The pharmacologic treatment of COPD is mainly conducted to relieve symptoms, to improve the lung functions, to reduce the occurrence of exacerbations, and health-related quality of life. Long-acting bronchodilators will continue to be the backbone of maintenance therapy and long-acting 2-agonist bronchodilators in the form of long-acting bronchodilator and long-acting muscarinic antagonist have been shown to be effective in airflow limitation and dyspnea reduction [4]. LABA combined with LAMA has additive bronchodilatory effects due to complementary mechanisms of action resulting in greater improvements in lung and symptom control in comparison to monotherapy [5]. Combination use of bronchodilators has thus become the first line of care to numerous patients with moderate COPD especially those with unremitting symptoms despite the use of single-agent treatment [6]. Combination of LABA and LAMA have been demonstrated in large randomized trials and real-life studies to result in better forced expiratory volume in one second (FEV 1), less use of rescue medication, and better patient-reported outcomes without a significant increase in adverse events [7]. Notably, this regime does not expose the patient to corticosteroids which have been linked to a number of clinically relevant complications

LABA, LAMA, and inhaled corticosteroids (ICS) are recommended as triple therapy traditionally in patients with a more severe disease or with frequent exacerbations despite optimization of bronchodilation [8]. The evidence behind the inclusion of ICS is its anti-inflammatory properties, especially in those patients with eosinophilic airway inflammation or recurring attacks [9]. But the advantage of ICS in COPD is not universal and its success does not seem to be associated with the entire population of COPD. Guideline-based recommendations notwithstanding, there is the increasing use of triple therapy in patients with moderate COPD in clinical practice [10]. This progression tends to happen at an early stage in the disease course, with no history of exacerbation or biomarker prescriptions. The practice of this kind is associated with the problem of overtreatment, unnecessary expenditure of health care resources, and preventable adverse effects of corticosteroids. Various investigations have always shown that there existed a high risk of pneumonia, oral candidiasis, dysphonia and possible systemic implications linked with prolonged use of ICS in COPD patients [11]. Whether there is a balance between possible benefits and harms of triple therapy in moderate COPD is still a controversial issue. Some of the studies have indicated a small-scale decrease in the rate of exacerbation using triple therapy, but some have noted no significant difference in symptoms and quality of life over single bronchodilator therapy [12][13].

Objective

- To compare the clinical effectiveness of dual bronchodilator therapy versus triple therapy in patients with moderate COPD.

METHODOLOGY

This was a comparative analytical study conducted at Imran Idrees teaching hospital Sialkot from May 2024 to May 2025, including 250 patients diagnosed with moderate chronic obstructive pulmonary disease (COPD).

Inclusion Criteria

- Patients of either gender aged 40 years and above
- Diagnosed cases of moderate COPD (GOLD stage II; FEV_1 50–79% predicted)
- Clinically stable disease with no acute exacerbation in the preceding four weeks
- Receiving regular maintenance inhalation therapy
- Patients willing to provide informed consent

Exclusion Criteria

- History of asthma or asthma–COPD overlap
- Recent acute exacerbation of COPD or respiratory infection
- Long-term systemic corticosteroid therapy
- Presence of other chronic respiratory diseases
- Severe cardiac, hepatic, or renal comorbidities
- Inability to perform acceptable spirometry
- Patients unwilling to participate

Data Collection

Data were collected using a structured proforma. Recorded variables included demographic characteristics such as age and gender, smoking history, duration of COPD, and current pharmacological therapy. Pulmonary function was assessed using spirometry, with forced expiratory volume in one second (FEV_1) expressed as percentage of predicted value. Symptom severity was evaluated using the COPD Assessment Test (CAT) score. Exacerbation history over the preceding year was documented based on clinical records. Treatment-related adverse events, including pneumonia and oral candidiasis, were also recorded. All assessments were performed following

standardized protocols to ensure accuracy and reproducibility.

Statistical Analysis

Data were analyzed using SPSS version 24.0. Quantitative variables such as age, FEV_1, CAT score, and exacerbation frequency were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Comparison between the dual therapy and triple therapy groups was performed using independent sample t-test for continuous variables and chi-square test for categorical variables. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

The mean age was 58.6 ± 8.4 years in the dual therapy group and 59.3 ± 8.9 years in the triple therapy group (p = 0.48), with males comprising 72.8% and 75.2% of patients, respectively (p = 0.66). Mean BMI was similar between groups at 25.1 ± 3.6 kg/m² for dual therapy and 25.4 ± 3.9 kg/m² for triple therapy (p = 0.52). Smoking exposure averaged 31.8 ± 11.2 pack-years in the dual therapy group and 33.1 ± 12.0 pack-years in the triple therapy group (p = 0.37). The mean duration of COPD was 6.1 ± 2.7 years versus 6.4 ± 2.9 years (p = 0.41), while baseline FEV_1 was 62.7 ± 5.8% and 63.0 ± 6.1% predicted, respectively (p = 0.69), indicating well-matched groups at study entry.

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants (N = 250)

Variable	Dual Therapy (n = 125)	Triple Therapy (n = 125)	p-value
Age (years), mean ± SD	58.6 ± 8.4	59.3 ± 8.9	0.48
Male gender, n (%)	91 (72.8)	94 (75.2)	0.66
BMI (kg/m²), mean ± SD	25.1 ± 3.6	25.4 ± 3.9	0.52
Smoking history (pack-years), mean ± SD	31.8 ± 11.2	33.1 ± 12.0	0.37
Duration of COPD (years), mean ± SD	6.1 ± 2.7	6.4 ± 2.9	0.41
Baseline FEV_1 (% predicted), mean ± SD	62.7 ± 5.8	63.0 ± 6.1	0.69

Follow-up FEV_1 increased from 62.7 ± 5.8% to 65.9 ± 6.3% in the dual therapy group and from 63.0 ± 6.1% to 68.4 ± 6.8% in the triple therapy group (p = 0.01). The absolute FEV_1 improvement was 3.2 ± 1.5% with dual therapy compared to 5.4 ± 2.0% with triple therapy (p < 0.001). Symptom severity, assessed by CAT score, improved from 18.5 ± 4.3 to 14.2 ± 3.7 in the dual therapy group and from 18.9 ± 4.1 to 13.6 ± 3.5 in the triple therapy group (p = 0.19), with mean CAT score reductions of 4.3 ± 2.1 and 5.3 ± 2.4 points, respectively (p = 0.03).

Table 2. Pulmonary Function and Symptom Severity Outcomes

Parameter	Dual Therapy	Triple Therapy	p-value
Baseline FEV_1 (% predicted)	62.7 ± 5.8	63.0 ± 6.1	0.69
Follow-up FEV_1 (% predicted)	65.9 ± 6.3	68.4 ± 6.8	0.01
Absolute FEV_1 improvement	3.2 ± 1.5	5.4 ± 2.0	<0.001
CAT score (baseline)	18.5 ± 4.3	18.9 ± 4.1	0.56
CAT score (follow-up)	14.2 ± 3.7	13.6 ± 3.5	0.19
Mean CAT score reduction	4.3 ± 2.1	5.3 ± 2.4	0.03

The annual exacerbation rate was 1.4 ± 0.6 episodes in the dual therapy group and 1.0 ± 0.5 episodes in the triple therapy group (p = 0.002). At least one exacerbation occurred in 57.6% of patients receiving dual therapy compared to 43.2% receiving triple therapy (p = 0.02), while two or more exacerbations were observed in 30.4% and 17.6% of

patients, respectively (p = 0.01). Exacerbation-related hospitalizations were numerically higher in the dual therapy group (16.8%) than in the triple therapy group (11.2%), though this difference did not reach statistical significance (p = 0.18). A good clinical response was achieved in 54.4% of patients on dual therapy and 65.6% on triple therapy (p = 0.07).

Table 3. Exacerbation Profile and Clinical Response

Outcome	Dual Therapy	Triple Therapy	p-value
Annual exacerbation rate (mean ± SD)	1.4 ± 0.6	1.0 ± 0.5	0.002
Patients with ≥1 exacerbation, n (%)	72 (57.6)	54 (43.2)	0.02
Patients with ≥2 exacerbations, n (%)	38 (30.4)	22 (17.6)	0.01
Exacerbation-related hospitalizations, n (%)	21 (16.8)	14 (11.2)	0.18
Good clinical response*, n (%)	68 (54.4)	82 (65.6)	0.07

*Good clinical response defined as improvement in FEV_1 ≥5%, CAT score reduction ≥3 points, and no exacerbation during follow-up.

Pneumonia occurred in 11.2% of the triple therapy group compared to 3.2% of the dual therapy group (p = 0.01), while oral candidiasis was reported in 8.8% versus 1.6%, respectively (p = 0.006). Hoarseness was observed in 10.4% of patients on triple therapy compared to 4.0% on dual therapy (p = 0.04). Overall, any adverse event was documented in 24.8% of patients receiving triple therapy compared to 8.8% receiving dual therapy (p < 0.001).

Table 4. Treatment-Related Adverse Events and Therapy Outcomes

Outcome	Dual Therapy n (%)	Triple Therapy n (%)	p-value
Pneumonia	4 (3.2)	14 (11.2)	0.01
Oral candidiasis	2 (1.6)	11 (8.8)	0.006
Hoarseness	5 (4.0)	13 (10.4)	0.04
Any adverse event	11 (8.8)	31 (24.8)	<0.001
Treatment discontinuation due to side effects	3 (2.4)	12 (9.6)	0.01
Need for therapy escalation	19 (15.2)	7 (5.6)	0.01

DISCUSSION

This paper compared the clinical efficacy of the two-bronchodilator therapy and triple therapy in patients with moderate COPD and revealed that although triple therapy showed statistically significant better effects on lung function and exacerbation outcome, such effects were at a significantly increased cost. In baseline, the two treatment groups were similar in age, smoking exposure, duration of the disease, and lung functioning, which made the comparative outcome of the treatment reliable. Pulmonary performance showed a higher improvement in FEV1 as a result of triple therapy the compared dual therapy. The average growth rate in FEV 1 was 5.4 /2.0 percent in triple therapy group as compared to 3.2 /1.5 percent in dual therapy group and the values of FEV 1 at the follow-up were 68.4 /6.8 percent and 65.9 /6.3 percent, respectively. The same degree of improvement in lung function with triple therapy has been reported in earlier studies, in which inhaled corticosteroid added has had incremental bronchodilatory and anti-inflammatory effects. Nevertheless, it has also been observed previously that absolute improvements in FEV1 in moderate COPD are small and are not necessarily accompanied by significant functional benefits [14][15]. The CAT score of the symptom control was better in both groups with the changes of -4.3 ± 2.1 and -5.3 ± 2.4 in the dual and triple therapy groups respectively. In spite of statistically significant larger mean reduction when using triple therapy, the follow-up CAT scores were similar in both groups, 14.2 ± 3.7 and 13.6 ± 3.5 respectively. Past studies have also established that although slight levels of higher reduction in the symptom scores can be achieved with triple therapy, the total patient-reported improvement compared to dual bronchodilation can be minimal and clinically insignificant in moderate disease [16][17].

Triple therapy showed better exacerbation results as the annual exacerbation rate was 1.0 0.5 versus 1.4 0.6 episodes in the dual therapy group. Also, the percentage of patients with at least one exacerbation decreased by 57.6 to 43.2, and two (or more) exacerbation was also lower by 30.4 to 17.6. The results are congruent with the previous studies that indicated that exacerbations are decreased by inhaled corticosteroids and especially in patients with increased inflammatory load. Nevertheless, it has also been stressed in past studies that such an advantage is stronger in selected phenotypes and not as universal in the wider moderate COPD population [18]. Although there were these positive results, the heightened incidence of adverse events when using triple therapy was a high score. Pneumonia was seen in 11.2% of patients treated with triple therapy versus 3.2% with the dual therapy, oral candidiasis was seen in 8.8% versus 1.6% and hoarseness in 10.4 percent

versus 4.0. There were almost one-quarter events of the overall adverse events that reported in almost all patients who were on triple therapy (24.8%), and less than one in ten patients on dual therapy (8.8%). Such increases in ICS-related adverse effects, in particular, pneumonia, have been previously noted and are of concern about the unnecessary use of corticosteroids in moderate COPD [19].

Limitations

The single-center design and use of non-probability consecutive sampling may limit the generalizability of the findings. Biomarkers such as blood eosinophil counts were not assessed, preventing stratification of patients based on inflammatory phenotype and potentially obscuring subgroups that might derive greater benefit from inhaled corticosteroids. Exacerbation history was partly based on clinical records, which may be subject to recall or documentation bias. Additionally, the duration of follow-up may not have been sufficient to capture long-term outcomes and rare adverse events associated with prolonged inhaled corticosteroid use.

CONCLUSION

It is concluded that in patients with moderate chronic obstructive pulmonary disease, dual bronchodilator therapy provides effective symptom control and meaningful improvement in lung function with a more favorable safety profile compared to triple therapy. Although triple therapy demonstrated greater gains in FEV_1 and a reduction in exacerbation frequency, these benefits were modest and accompanied by a significantly higher incidence of treatment-related adverse events, particularly pneumonia and oral candidiasis

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