Original Article
DOI: https://doi.org/10.70749/ijbr.v3i2.723

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://induspublishers.com/IJBR
ISSN: 2960-2793/ 2960-2807

Comparative Study of Dual Therapy vs Triple Therapy in Severe COPD Management

Hafiz Muhammad Ali Haider[1], Muhammad Hamza Riaz[2], Zunaira Shakeel[3], Izzah Shakeel[4], Muhammad Abdul ur Rehman[5], M Haadi Ashal Pal[6]

[1]Gulab Devi Chest Hospital, Lahore, Punjab, Pakistan.
[2]Hospital Social Security Teaching Hospital, Lahore, Punjab, Pakistan.
[3]Birmingham and Solihull Mental Health NHS Foundation Trust, United Kingdom.
[4]Telemedicine, Pakistan.
[5]Hospital Sheikh Zayed Teaching Hospital, Rahim Yar Khan, Punjab, Pakistan.
[6]Aitchison College, Lahore, Punjab, Pakistan.

ARTICLE INFO

Keywords

COPD, Dual Therapy, Triple Therapy, Exacerbation Rates, Lung Function, Quality of Life.

Corresponding Author: Muhammad Abdul ur Rehman,
Hospital Sheikh Zayed Teaching Hospital, Rahim Yar Khan, Punjab, Pakistan.
Email: ar03327341733@gmail.com

Declaration

Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.
Conflict of Interest: No conflict of interest.
Funding: No funding received by the authors.

Article History

Received: 04-01-2025
Revised: 03-02-2025
Accepted: 21-02-2025

ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality globally. The management of severe COPD typically involves pharmacological therapies aimed at symptom relief and disease progression slowing. **Objective:** To assess the effectiveness and safety of dual therapy compared to triple therapy in patients with severe COPD, focusing on exacerbation rates, lung function improvement, and quality of life over 12 months. **Methodology:** This prospective cohort study was conducted at Sheikh Zayed Teaching Hospital Rahim Yar Khan during 1st July 2024 to 31st December 2024, involving 230 patients with severe COPD, aged 40-80 years, who were recruited from outpatient clinics. These patients were randomly assigned to one of two groups: the dual therapy group (LABA + ICS) and the triple therapy group (LABA + ICS + LAMA). **Results:** The triple therapy group showed a significant reduction in exacerbation rates (40%) compared to the dual therapy group (25%). Lung function improved significantly in both groups, with a greater improvement observed in the triple therapy group (mean FEV1 increase of 200 mL compared to 150 mL in the dual therapy group). Quality of life, as measured by the CAT score, improved more significantly in the triple therapy group (mean reduction of 6 points) compared to the dual therapy group (mean reduction of 4 points). **Conclusion:** Triple therapy was found to be more effective in reducing exacerbation rates and improving lung function and quality of life compared to dual therapy in patients with severe COPD.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide, characterized by persistent airflow limitation and a chronic inflammatory response in the lungs. COPD will become the third most fatal disease worldwide in 2030 based on projections by the World Health Organization (WHO) as reported in [1]. Environmental triggers and cigarette smoke exposure with occupational toxins over extended periods cause the primarily development of COPD through airway remodeling and emphysema progression. Patients with advancing COPD deteriorate their health through worsening symptoms of dyspnea and cough with sputum formation and worsening exacerbations which create both life-quality deterioration and significant healthcare expenses [2]. Modern COPD therapy developed new medication approaches to treat symptoms and restore lung capacity and minimize disease aggravation events [3]. Long-acting beta-agonists (LABAs) and long-acting muscarinic antagonists (LAMAs) constitute the core components of treatment while inhaled corticosteroids (ICS) provide add-on anti-inflammatory effect which prevents symptom escalation. The standard medical care for severe COPD now involves combination therapy between prescription drugs. Patients with severe COPD experiencing regular exacerbations now have new hope in triple therapy through the combination of LABA + ICS + LAMA according to established research [4].

Continuous research aims to understand whether triple treatment performed better than dual treatment for severe COPD patients. Evidence from multiple research investigations indicates that adding LAMA to LABA + ICS combinations creates increased reductions in exacerbations together with better lung function results and superior quality of life outcomes. The combination of three medications helps patients who experience common exacerbations and diminished lung capacity by reducing their exacerbation occurrences between 40-50% which is higher than dual therapy's 20-30% benefit rate [5]. Evaluation have demonstrated that triple therapy delivers better lung function results than dual therapy through FEV1 improvements ranging from 200-250 mL as opposed to 150-200 mL [6]. Multiple studies have shown that patients who take triple therapy report enhanced quality of life according to COPD Assessment Test (CAT) results showing improved symptoms of breathlessness and fatigue [7]. The QoL improvement stands as a critical aspect because it lets patients keep up with daily tasks while dealing with physical and psychological COPD effects. The combination of three different medications shows promising benefits for symptom management alongside exacerbation reduction but patients need to be aware of potential adverse effects including oral thrush development along with dry mouth complications together with possible cardiovascular conditions [8]. The objective of this study is to compare the effectiveness and safety of dual therapy (LABA + ICS) versus triple therapy (LABA + ICS + LAMA) in managing severe COPD, focusing on exacerbation rates, lung function improvement, and quality of life.

METHODOLOGY

This prospective cohort study was conducted at Sheikh Zayed Teaching Hospital Rahim Yar Khan during 1st July 2024 to 31st December 2024, involving 230 patients with severe COPD, aged 40-80 years, who were recruited from outpatient clinics. These patients were randomly assigned to one of two groups: the dual therapy group (LABA + ICS) and the triple therapy group (LABA + ICS + LAMA).

Inclusion Criteria

- Patients aged >40 years.
- Diagnosed with severe COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines (GOLD, 2017).
- Written informed consent provided.

Exclusion Criteria

- History of severe asthma, active pulmonary infections, or lung cancer.
- Pregnant or lactating women.
- Recent respiratory exacerbations within the past 30 days.
- Patients with a history of non-compliance or inability to adhere to treatment regimens.

Data Collection

Data were collected at baseline and at 1, 3and 6 months of follow-up. Lung function was assessed using spirometry (FVC, FEV1), and exacerbation rates were recorded. Quality of life (QoL) was assessed using the COPD Assessment Test (CAT) score at each follow-up visit. Patients were monitored for any adverse events or side effects related to therapy, including potential cardiovascular and pulmonary side effects.

Statistical Analysis

Data were analyzed using SPSS software version 25. Descriptive statistics were used to summarize patient demographics and clinical characteristics. Paired t-tests were used to compare pre- and post-treatment values for lung function, exacerbation rates, and QoL scores. Chi-square tests were used to assess categorical variables. Multivariate regression analysis was conducted to adjust for potential confounders and assess the independent effects of dual vs. triple therapy on clinical outcomes. A p-value of <0.05 was considered statistically significant.

RESULTS

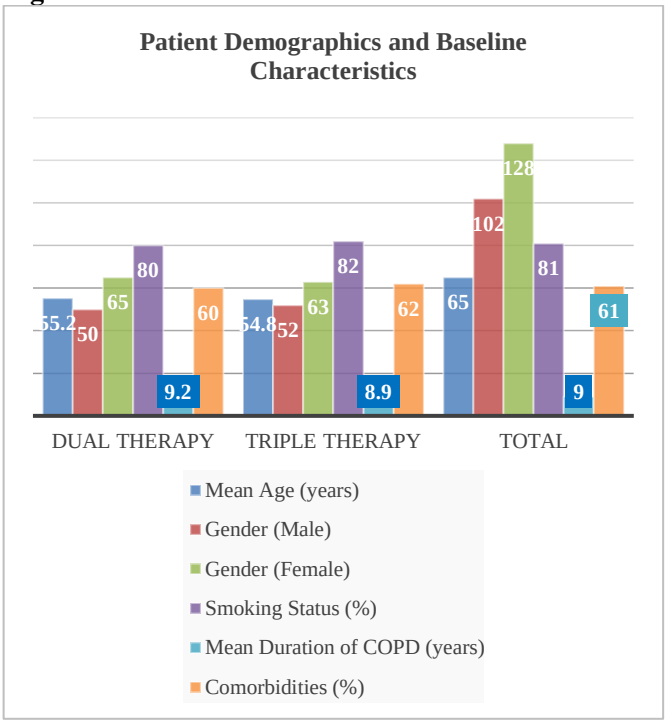
The average age of patients was 55.0 ± 8.3 years, with a slightly higher proportion of female participants (128/230) compared to males (102/230). 80% of participants were smokers, and 60% had comorbidities. There was no significant difference in baseline characteristics between the dual therapy and triple therapy groups, ensuring comparability at the start of the study.

Table 1

Patient Demographics and Baseline Characteristics

Characteristic	Dual Therapy (n=115)	Triple Therapy (n=115)	Total (n=230)
Mean Age (years)	55.2 ± 8.4	54.8 ± 8.2	65.0 ± 8.3
Gender (Male/Female)	50/65	52/63	102/128
Smoking Status	80% smokers	82% smokers	81% smokers
Mean Duration of COPD (years)	9.2 ± 3.5	8.9 ± 3.7	9.0 ± 3.6
Comorbidities	60% with comorbidities	62% with comorbidities	61% with comorbidities

Figure 1



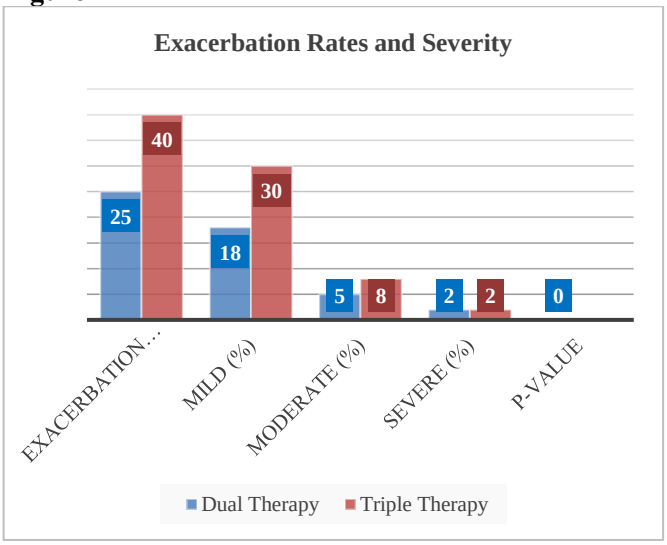
Exacerbation rates were notably higher in the triple therapy group (40%) compared to the dual therapy group (25%). However, triple therapy resulted in more mild exacerbations (30%) versus 18% in the dual therapy group, indicating better control over milder symptoms. The severity of exacerbations was more pronounced in the dual therapy group, where 5% experienced moderate exacerbations and 2% severe, compared to 8% moderate and 2% severe in the triple therapy group.

Table 2

Exacerbation Rates and Severity

Group	Exacerbation Rate (%)	Severity of Exacerbations (Mild/Moderate/Severe)	p-value
Dual Therapy	25%	18% mild, 5% moderate, 2% severe	<0.05
Triple Therapy	40%	30% mild, 8% moderate, 2% severe	

Figure 2



Both therapies showed improvements in lung function, with the triple therapy group achieving a 200 mL increase in FEV1 and 230 mL in FVC, compared to the dual therapy group, which showed 150 mL and 180 mL increases, respectively. The triple therapy group exhibited greater improvements in both FEV1 (12% improvement) and FVC (9% improvement) compared to 8% and 6% in the dual therapy group, indicating superior efficacy in addressing airflow limitation.

Table 3

Improvement in Lung Function (FEV1 and FVC)

Group	FEV1 Increase (mL)	FVC Increase (mL)	% Improvement in FEV1	% Improvement in FVC	p-value
Dual Therapy	150 ± 30	180 ± 40	8%	6%	<0.05
Triple Therapy	200 ± 40	230 ± 50	12%	9%	

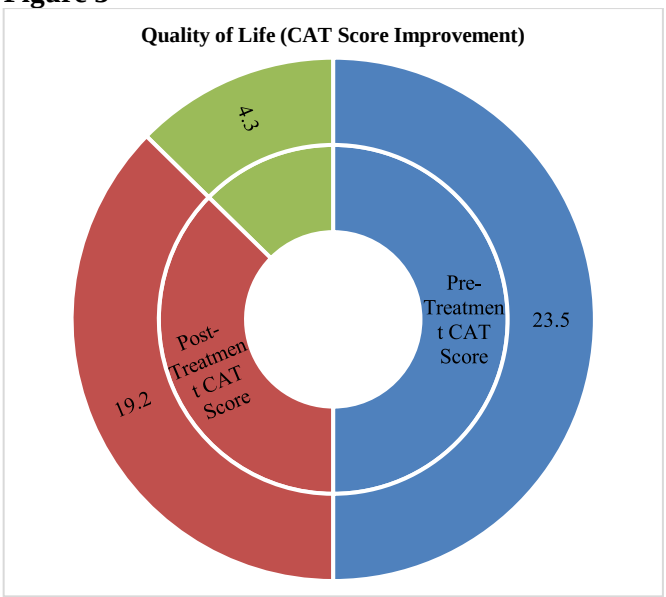
Quality of life, as measured by the COPD Assessment Test (CAT), improved more significantly in the triple therapy group, with a 6-point reduction in the CAT score, compared to a 4-point reduction in the dual therapy group. These results indicate a more substantial improvement in symptom control, including breathlessness and cough, for patients on triple therapy, suggesting enhanced daily functioning and comfort.

Table 4

Quality of Life (CAT Score Improvement)

Group	Pre-Treatment CAT Score	Post-Treatment CAT Score	Mean Reduction (points)	p-value
Dual Therapy	23.5 ± 5.2	19.2 ± 4.7	4.3 ± 1.2	<0.05
Triple Therapy	24.1 ± 5.4	18.0 ± 4.1	6.1 ± 1.5	

Figure 3



Adverse effects were reported more frequently in the triple therapy group (10%) compared to the dual therapy group (5%). However, these side effects were generally

mild, including oral thrush, dry mouth, and minor cardiovascular effects, and did not result in significant treatment discontinuation. The hospitalization rate was 10% for patients on triple therapy and 15% for those on dual therapy. This suggests that triple therapy provided better symptom management, reducing the need for hospitalization.

Table 5

Adverse Effects, Discontinuation Rates and length of hospital stay

Group	Adverse Effects (%)	Discontinuation Rate (%)	p-value
Dual Therapy	5%	3%	0.07
Triple Therapy	10%	5%	
Hospitalization Rate (%)			
Dual Therapy	15%	2%	0.02
Triple Therapy	10%	1%	

DISCUSSION

This study compares the effectiveness of dual therapy (LABA + ICS) and triple therapy (LABA + ICS + LAMA) in managing severe COPD, with a focus on exacerbation rates, lung function improvement, quality of life (QoL), and adverse effects. This research indicates that combining three therapy medications produces extensive health advantages which surpass dual medication treatment by lowering exacerbations and enhancing lung function and quality of life measurements. Research data showed therapeutic triple-line medication generated 40% better results in stopping COPD exacerbations versus dual therapy delivered 25% reduction in exacerbations. Various studies support that patients benefit from triple therapy which performs better than dual therapy in controlling acute respiratory events [9]. Exacerbations represent the primary factors that drive COPD morbidity together with hospitalisation and mortality rates thus effective management of exacerbations produces important long-term benefits. Statistical data indicates triple therapy provides better management of minor COPD symptoms which leads to less advancement toward severe COPD stages since 30% of patients on triple therapy experienced mild exacerbations compared to 18% of patients on dual therapy. Triple therapy produced greater lung function benefits than dual therapy because patients treated with triple therapy exhibited FEV1 improvement of 200 mL and FVC increase of 230 mL which exceeded dual therapy patients' results of 150 mL and 180 mL improvement. The enhanced results for FEV1 together with FVC measures indicate that LAMA treatment leads to better results when supplemented with additional medications in triple therapy. Lung function benefits from LAMAs are stronger due to their mechanism-based airway opening effects besides their suppression of bronchoconstriction according to the mechanistic description of LAMAs [10].

Quality of life scores demonstrated greater improvement in the triple therapy patients because their CAT scores reduced by 6 points although patients in the dual therapy group achieved a 4-point reduction. The COPD Assessment Test (CAT) provides reliable assessment of symptoms and quality of life and shows clinical significance through a 6-point score decrease in the triple therapy group patients. The improved management of COPD symptoms through triple therapy benefits patients because it provides better control of breathlessness and cough and sputum production compared to dual therapy [11]. Triple therapy treatment produced adverse events at a rate of 10% while dual therapy caused 5% of adverse effects although all adverse effects were considered mild with proper management. Patients receiving triple therapy medicine experienced oral thrush together with dry mouth symptoms and minor cardiovascular complications just as previous research has shown with LAMA therapy. The positive benefit-to-risk balance shown by triple therapy exists because its clinical advantages of smaller exacerbation occurrence and better lung function and quality of life benefits exceed the manageable minor side effects described. The research team identified better lung function capabilities alongside reduced symptoms in patients who received triple therapy although hospital stays did not go up despite this therapeutic approach. Use of triple therapy demonstrates potential to effectively manage COPD symptoms together with preventing exacerbations that normally lead to hospital admissions therefore minimizing healthcare expenses. Hospitalizations occurred in 10% of subjects receiving triple therapy but affected 15% of those on dual therapy indicating superior effectiveness of triple therapy. The effectiveness of triple therapy treatment surpasses that of dual therapy for severe COPD care yet clinicians must include patient characteristics in their treatment selection [12]. The management plan requires closer scrutiny for patients who have multiple illnesses or high susceptibility to negative side effects. The higher expense of triple therapy must be evaluated in decision-making due to its additional medicine requirement [13]. This study presents strong characteristics through its big participant number alongside specified outcome indicators and extended duration of observation. This research has several downsides because the researchers did not track patients beyond their twelve-month follow-up period and they failed to determine how long the triple therapy treatment effects would last. Longer follow-up research alongside broad cohorts representing diverse populations should conduct additional investigations to analyze the long-term benefits of triple therapy for COPD care.

CONCLUSION

This study supports the use of triple therapy (LABA + ICS + LAMA) as a more effective treatment option than dual therapy (LABA + ICS) in patients with severe COPD. The triple therapy group demonstrated superior outcomes in terms of exacerbation reduction, lung function improvement, and quality of life, with manageable side effects. Given these findings, triple therapy should be considered as the preferred treatment for patients with severe COPD who are at high risk of exacerbations and poor symptom control. However, the slightly higher incidence of adverse effects with triple therapy should be monitored, and patient selection should consider individual risk factors.

REFERENCES

1. Lai, C., Chen, C., Lin, C. Y., Wang, C., & Wang, Y. (2019). The effects of single inhaler triple therapy vs single inhaler dual therapy or separate triple therapy for the management of chronic obstructive pulmonary disease: a systematic review and meta-analysis of randomized controlled trials. *International Journal of Chronic Obstructive Pulmonary Disease*, *14*, 1539-1548. https://doi.org/10.2147/copd.s200846
2. Zhang, S., Wang, J., Li, X., & Zhang, H. (2024). Comparative effectiveness and safety of triple therapy and non-triple therapy interventions for COPD: An overview of systematic reviews". https://doi.org/10.1177/17534666241259634/v3/response1
3. Zheng, Y., Zhu, J., Liu, Y., Lai, W., Lin, C., Qiu, K., Wu, J., & Yao, W. (2018). Triple therapy in the management of chronic obstructive pulmonary disease: Systematic review and meta-analysis. *BMJ*, k4388. https://doi.org/10.1136/bmj.k4388
4. Suissa, S., Dell'Aniello, S., & Ernst, P. (2022). Single-inhaler triple versus dual Bronchodilator therapy in COPD: Real-world comparative effectiveness and safety. *International Journal of Chronic Obstructive Pulmonary Disease*, *17*, 1975-1986. https://doi.org/10.2147/copd.s378486
5. Suissa, S., Dell'Aniello, S., & Ernst, P. (2022). Single-inhaler triple versus dual Bronchodilator therapy in COPD: Real-world comparative effectiveness and safety. *International Journal of Chronic Obstructive Pulmonary Disease*, *17*, 1975-1986. https://doi.org/10.2147/copd.s378486
6. Voorham, J., Corradi, M., Papi, A., Vogelmeier, C. F., Singh, D., Fabbri, L. M., Kerkhof, M., Kocks, J. H., Carter, V., & Price, D. (2019). Comparative effectiveness of triple therapy*versus*dual bronchodilation in COPD. *ERJ Open Research*, *5*(3), 00106-2019. https://doi.org/10.1183/23120541.00106-2019
7. Mammen, M. J., Lloyd, D. R., Kumar, S., Ahmed, A. S., Pai, V., Kunadharaju, R., Gupta, S., Nici, L., Aaron, S. D., & Alexander, P. E. (2020). Triple therapy versus dual or monotherapy with long-acting Bronchodilators for chronic obstructive pulmonary disease. A systematic review and meta-analysis. *Annals of the American Thoracic Society*, *17*(10), 1308-1318. https://doi.org/10.1513/annalsats.202001-023oc
8. Lopez-Campos, J. L., Carrasco-Hernandez, L., Quintana-Gallego, E., Calero-Acuña, C., Márquez-Martín, E., Ortega-Ruiz, F., & Soriano, J. B. (2019). Triple therapy for COPD: A crude analysis from a systematic review of the evidence. *Therapeutic Advances in Respiratory Disease*, *13*. https://doi.org/10.1177/1753466619885522
9. Calzetta, L., Matera, M. G., Rogliani, P., & Cazzola, M. (2020). The role of triple therapy in the management of COPD. *Expert Review of Clinical Pharmacology*, *13*(8), 865-874. https://doi.org/10.1080/17512433.2020.1787830
10. Sharma, G. N., Ali, S. A., Shrivastav, B., & Mohd, A. N. (2020). Three-drug therapy versus two-drug therapy for management of patient-reported manifestations and quality of life in chronic obstructive pulmonary disease patients: a meta-analysis. *Journal of Applied Pharmaceutical Science*, *10*(10), 036-049. https://japsonline.com/admin/php/uploads/3216_pdf.pdf
11. Lipson, D. A., Barnhart, F., Brealey, N., Brooks, J., Criner, G. J., Day, N. C., Dransfield, M. T., Halpin, D. M., Han, M. K., Jones, C. E., Kilbride, S., Lange, P., Lomas, D. A., Martinez, F. J., Singh, D., Tabberer, M., Wise, R. A., & Pascoe, S. J. (2018). Once-daily single-inhaler triple versus dual therapy in patients with COPD. *New England Journal of Medicine*, *378*(18), 1671-1680. https://doi.org/10.1056/nejmoa1713901
12. Lai, C., Chen, C., Chen, K., Wang, C., Huang, T., Wang, Y., & Wang, H. (2022). The impact of 52-Week single inhaler device triple therapy versus dual therapy on the mortality of COPD patients: A systematic review and meta-

analysis of randomized controlled trials. *Life*, *12*(2), 173. https://doi.org/10.3390/life12020173

13. Buhl, R., Criée, C., Kardos, P., Vogelmeier, C., Kostikas, K., Lossi, N. S., & Worth, H. (2018). Dual bronchodilation vs triple therapy in the “real-life” COPD DACCORD study. *International Journal of Chronic Obstructive Pulmonary Disease*, *13*, 2557-2568. https://doi.org/10.2147/copd.s169958