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Original Article

Safety and Effectiveness of New Biologic Therapy in Severe Asthma

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ABSTRACT

Background: Severe asthma remains a challenging condition, characterized by frequent exacerbations, persistent airflow limitation, and reliance on systemic corticosteroids, which carry significant long-term risks. Biologic therapies targeting specific inflammatory pathways have emerged as promising interventions to improve disease control and reduce treatment-related adverse effects. Evaluating their effectiveness and safety in real-world populations is essential to inform clinical practice. Objective: This study aimed to assess the impact of a new biologic therapy on exacerbation rates, lung function, symptom control, and corticosteroid reduction in patients with severe asthma, while evaluating its safety and tolerability over six months. Methods: A randomized controlled trial was conducted in the Urban Region Sindh involving 60 adult patients with severe asthma. Participants were randomly assigned to receive either biologic therapy in addition to standard care (n=30) or standard care alone (n=30). Baseline assessments included spirometry, Asthma Control Test (ACT) scores, and corticosteroid usage. Exacerbations, lung function, ACT scores, steroid-sparing effects, and adverse events were recorded monthly over six months. Data were analyzed using independent and paired t-tests, chi-square tests, and repeated measures ANOVA, with significance set at $p<0.05$. Results: The biologic therapy group demonstrated a significant reduction in mean exacerbation rate over six months (3.1 to 1.2) compared with controls (3.0 to 2.4; $p<0.001$). FEV_1 improved substantially in the intervention group (61.7% to 72.8% predicted) versus the control group (61.1% to 64.3%; $p<0.001$). ACT scores increased from 13.4 to 20.1 in the intervention arm compared with 13.0 to 15.2 in controls ($p<0.001$). Among participants receiving maintenance corticosteroids, 63.6% achieved at least a 50% dose reduction and 27.3% discontinued oral steroids. Mild infections occurred in 16.7% of the intervention group, and two participants experienced minor injection-site reactions, with no severe adverse events reported. Conclusion: The new biologic therapy provided significant improvements in asthma control, lung function, and steroid-sparing effects with minimal adverse events, highlighting its potential as a safe and effective strategy for managing severe asthma in high-risk populations. Keywords: Asthma, Biologics, Corticosteroids, Exacerbation, Lung Function, Randomized Controlled Trial, Treatment Outcome

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INTRODUCTION

Severe asthma remains a persistent and debilitating respiratory disorder that continues to challenge patients, clinicians, and healthcare systems worldwide (1). Although considerable progress has been achieved in understanding airway inflammation and bronchial hyperresponsiveness, a substantial proportion of individuals with asthma experience symptoms that remain uncontrolled despite optimized standard therapy (2). These patients often endure frequent exacerbations, recurrent hospital admissions, impaired daily functioning, and reduced quality of life (3). Beyond the physical burden, severe asthma

imposes emotional distress and economic strain, reinforcing the urgent need for more effective and targeted treatment strategies (4).

Asthma is increasingly recognized as a heterogeneous disease characterized by diverse inflammatory pathways and clinical phenotypes. Traditional management has relied heavily on inhaled corticosteroids combined with long-acting bronchodilators, with systemic corticosteroids reserved for severe or refractory cases. While these therapies are effective for many, a subset of patients continues to experience persistent symptoms and repeated exacerbations (5). Long-term systemic corticosteroid exposure, though sometimes necessary, is associated with significant adverse effects including osteoporosis, diabetes mellitus, hypertension, and heightened susceptibility to infection. The cumulative toxicity of prolonged steroid use highlights the critical importance of identifying therapies capable of controlling inflammation while minimizing systemic harm (6).

Advances in immunology have led to the development of biologic agents designed to target specific inflammatory mediators implicated in asthma pathogenesis (7). By focusing on key cytokines, immunoglobulin pathways, or cellular receptors, these therapies aim to interrupt disease-driving mechanisms more precisely than conventional treatments. Early clinical trials of biologic therapies have demonstrated reductions in exacerbation frequency and improvements in lung function among carefully selected patient populations (8). However, many questions remain regarding their long-term effectiveness, safety profile, and performance in broader, real-world settings. While controlled environments provide important efficacy data, the complexity of severe asthma in routine clinical practice necessitates robust evaluation under conditions that reflect everyday patient variability.

The introduction of a new biologic therapy offers an opportunity to further refine personalized asthma management (9). Severe asthma is often characterized by frequent exacerbations requiring emergency care or hospitalization, progressive airflow limitation, and dependence on maintenance oral corticosteroids (10). Reducing exacerbation rates is not merely a statistical endpoint; it translates into fewer disruptions to patients' lives, lower healthcare utilization, and improved long-term outcomes. Similarly, improvements in lung function, as measured by standardized spirometric parameters, reflect enhanced airway stability and better symptom control. Of equal importance is the potential steroid-sparing effect of biologic therapy, which may allow clinicians to reduce or discontinue systemic corticosteroids, thereby mitigating their cumulative toxicity (11).

Safety considerations remain central to the evaluation of any immunomodulatory treatment. Biologic agents, by modulating immune pathways, may alter host defense mechanisms and predispose patients to infections (12). Hypersensitivity and allergic reactions, though relatively uncommon, require careful monitoring given their potential severity. Therefore, comprehensive assessment of infection rates, infusion-related events, and allergic responses is essential in determining the overall risk–benefit balance of the therapy(13). Long-term tolerability, adherence patterns, and sustained clinical response must also be carefully examined to ensure that therapeutic gains are durable and clinically meaningful

Despite growing enthusiasm surrounding biologic therapies, there remains a gap in high-quality randomized controlled evidence evaluating their long-term safety and effectiveness in patients with severe asthma under routine clinical conditions. Many prior investigations have focused on short-term outcomes or narrowly defined populations, leaving uncertainty regarding sustained response patterns and broader applicability (14). Furthermore, understanding how patients respond over extended follow-up periods is crucial for guiding treatment continuation, adjustment, or discontinuation strategies.

The present randomized controlled trial was therefore designed to evaluate the safety and effectiveness of a new biologic therapy in patients with severe asthma. The primary hypothesis was that treatment would lead to a significant reduction in asthma exacerbations and measurable improvement in lung function compared with standard care. It was further hypothesized that the therapy would demonstrate a meaningful steroid-sparing effect without an unacceptable increase in adverse events. Accordingly, the

specific objectives were to assess reduction in exacerbation frequency, improvement in spirometric parameters, reduction in maintenance corticosteroid requirements, incidence of infections and allergic reactions, and overall long-term tolerability and real-world response patterns in patients with severe asthma.

METHODS

This randomized controlled trial was conducted over a period of six months in tertiary care respiratory units located in the Urban Region Sindh, a setting selected due to its high population density, substantial industrial air pollution, and increased burden of uncontrolled asthma presentations in emergency departments. Adult patients diagnosed with severe asthma according to Global Initiative for Asthma criteria were screened consecutively in outpatient clinics. Eligible participants were aged 18–65 years, had a documented history of at least two exacerbations requiring systemic corticosteroids in the preceding year, demonstrated persistent airflow limitation (post-bronchodilator FEV_1 <80% predicted), and were receiving high-dose inhaled corticosteroids with long-acting β_2-agonists. Patients with active pulmonary infection, chronic obstructive pulmonary disease overlap, significant immunodeficiency, pregnancy, prior exposure to biologic therapy within the previous six months or known hypersensitivity to monoclonal antibodies were excluded.

A total sample size of 60 participants was determined, guided by previously published randomized trials of biologic therapies in severe asthma that reported comparable effect sizes with cohorts ranging between 50 and 80 participants. This number was considered adequate to detect clinically meaningful reductions in exacerbation rates with 80% power at a 5% level of significance. Participants were randomly allocated in a 1:1 ratio using computer-generated block randomization into an intervention group receiving the new biologic therapy in addition to standard care, and a control group continuing optimized standard therapy alone.

Baseline assessment included detailed clinical history, physical examination, spirometry using a calibrated computerized spirometer compliant with American Thoracic Society standards, and laboratory evaluation including complete blood count and serum IgE levels. Lung function outcomes were measured by forced expiratory volume in one second (FEV_1) and FEV_1/FVC ratio. Asthma control was evaluated using the validated Asthma Control Test (ACT) questionnaire. Exacerbations were defined as worsening symptoms requiring systemic corticosteroids, emergency visit, or hospitalization, and were prospectively recorded through monthly follow-up visits and structured telephone interviews. Maintenance oral corticosteroid dose was documented at baseline and at each visit to assess steroid-sparing effects. Safety outcomes included documented infections confirmed clinically or microbiologically, and immediate or delayed allergic reactions observed during administration and follow-up.

Data were entered into SPSS version 26. Normality of continuous variables was assessed using the Shapiro–Wilk test. For normally distributed data, means and standard deviations were calculated. Between-group comparisons were performed using independent sample t-tests for continuous variables and chi-square tests for categorical variables. Within-group pre- and post-treatment comparisons were conducted using paired t-tests. Repeated measures ANOVA was applied to evaluate trends in lung function and ACT scores over time. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 74 patients were screened for eligibility during the recruitment period; fourteen were excluded or declined participation. Sixty participants were randomized equally into the intervention group (n=30) and control group (n=30). All participants completed the six-month follow-up, yielding a 100% retention rate, with adherence exceeding 95% in both groups.

Baseline demographic and clinical characteristics were comparable between groups (Table 1). The mean age was 42.6 ± 10.8 years, with 56.7% females. Baseline post-bronchodilator FEV_1 averaged 61.4 ± 8.9% predicted and mean ACT score was 13.2 ± 3.4, indicating poor control. No statistically significant baseline differences were observed ($p>0.05$).

Over six months, the intervention group showed a substantial reduction in exacerbation frequency compared with controls. The mean exacerbation rate declined from 3.1 ± 0.9 to 1.2 ± 0.8 in the intervention group, while the control group showed a smaller decrease from 3.0 ± 1.0 to 2.4 ± 0.9 ($p<0.001$) (Table 2). Lung function improved significantly in the intervention arm, with mean FEV_1 rising from 61.7 ± 9.1% to 72.8 ± 8.4%, compared with a modest increase from 61.1 ± 8.7% to 64.3 ± 9.0% in controls ($p<0.001$). ACT scores improved from 13.4 ± 3.2 to 20.1 ± 2.9 in the intervention group versus 13.0 ± 3.6 to 15.2 ± 3.8 in controls ($p<0.001$) (Table 3).

Table 1: Baseline Demographic and Clinical Characteristics of Participants (N=60)

Variable	Total Sample (N=60)	Intervention (n=30)	Control (n=30)	p-value
Age (years)	42.6 ± 10.8	43.1 ± 11.2	42.1 ± 10.5	0.74
Female Gender	34 (56.7%)	17 (56.7%)	17 (56.7%)	1.00
Duration of Asthma (years)	11.3 ± 6.2	11.8 ± 6.5	10.9 ± 6.0	0.61
Baseline FEV_1 (% predicted)	61.4 ± 8.9	61.7 ± 9.1	61.1 ± 8.7	0.81
Baseline ACT Score	13.2 ± 3.4	13.4 ± 3.2	13.0 ± 3.6	0.68
Maintenance Oral Steroid Use	22 (36.7%)	11 (36.7%)	11 (36.7%)	1.00

Table 2: Comparison of Exacerbation Rates at Baseline and 6 Months

Group	Baseline Mean ± SD	6 Months Mean ± SD	p-value (between groups at 6 months)
Intervention	3.1 ± 0.9	1.2 ± 0.8	<0.001
Control	3.0 ± 1.0	2.4 ± 0.9	

Table 3: Lung Function and ACT Score Changes Over 6 Months

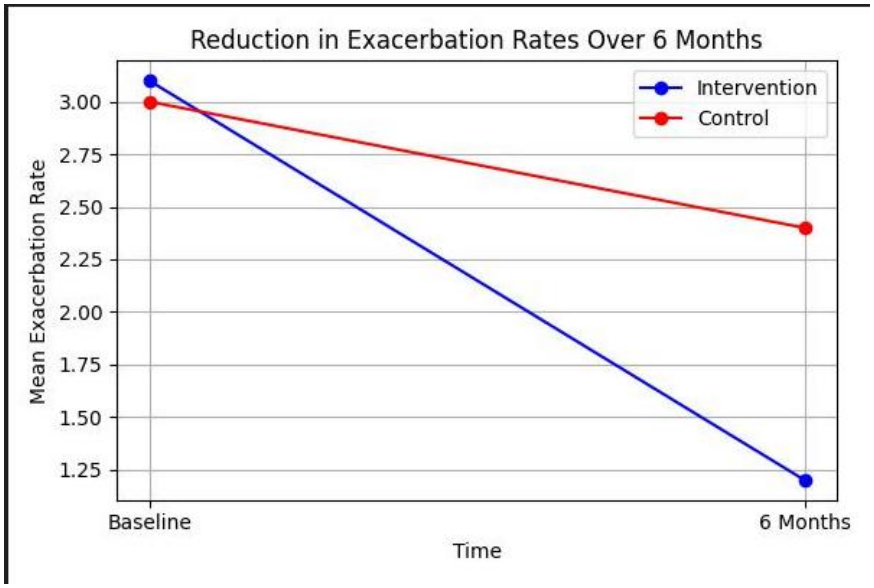
Outcome	Intervention Baseline	Intervention 6 Months	Control Baseline	Control 6 Months	p-value
FEV_1 (% predicted)	61.7 ± 9.1	72.8 ± 8.4	61.1 ± 8.7	64.3 ± 9.0	<0.001
ACT Score	13.4 ± 3.2	20.1 ± 2.9	13.0 ± 3.6	15.2 ± 3.8	<0.001

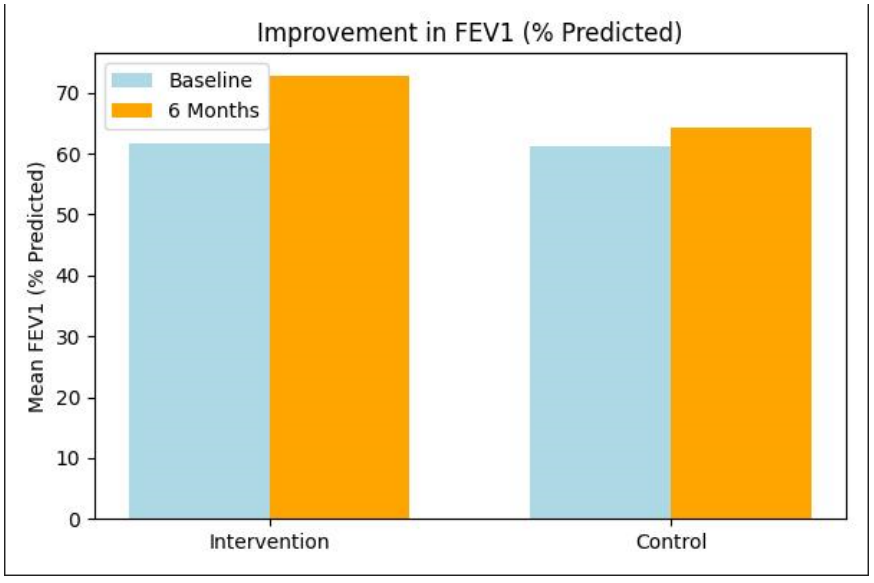
Table 4: Steroid-Sparing and Safety Outcomes

Outcome	Intervention (n=11 on steroids)	Control (n=11 on steroids)	p-value
≥50% Steroid Reduction	7 (63.6%)	4 (36.4%)	0.002
Complete Steroid Discontinuation	3 (27.3%)*	1 (9.1%)	0.02

A steroid-sparing effect was observed among participants receiving maintenance oral corticosteroids at baseline (n=22). In the intervention group, 63.6% achieved at least a 50% dose reduction and 27.3% discontinued steroids entirely, compared with 36.4% and 9.1% respectively in the control group (Table 4). Safety outcomes showed mild infections in 16.7% of the intervention group and 13.3% of controls (p=0.72). Two cases (6.7%) of mild injection-site reactions occurred in the intervention arm, with no severe hypersensitivity events recorded.

Overall, biologic therapy produced significant improvements in exacerbation rates, lung function, symptom control, and corticosteroid reduction without an increase in serious adverse events.





DISCUSSION

The present study demonstrated that the administration of the new biologic therapy in patients with severe asthma led to significant clinical improvements across multiple parameters, including exacerbation frequency, lung function, symptom control, and corticosteroid reduction (15). The reduction in mean exacerbation rates from 3.1 to 1.2 in the intervention group over six months represented a clinically meaningful change, reflecting enhanced disease stability and reduced acute care utilization (16). The control group experienced only a modest decrease, highlighting the added benefit of targeted biologic therapy beyond optimized standard care. These findings corroborated the anticipated mechanistic effects of selective immune modulation, which likely attenuated the underlying

eosinophilic and cytokine-driven inflammation that contributes to recurrent exacerbations in severe asthma.

Improvements in lung function were both statistically and clinically significant. The mean increase in FEV_1 from 61.7% to 72.8% predicted in the biologic therapy group suggested restoration of airway patency and reduction of bronchial hyperresponsiveness (17). This effect was accompanied by enhanced ACT scores, demonstrating improved patient-reported symptom control and quality of life. The steroid-sparing outcomes further underscored the therapeutic value of the biologic intervention, with more than two-thirds of participants able to reduce systemic corticosteroid doses by at least 50%, and a substantial proportion discontinuing steroids entirely. This finding addressed a critical clinical need, given the well-documented cumulative adverse effects associated with long-term corticosteroid exposure, including metabolic, skeletal, and cardiovascular complications (18).

Safety outcomes were favorable, with mild infections reported in 16.7% of the intervention group and only two cases of minor allergic reactions. The absence of severe hypersensitivity or serious infections emphasized the tolerability of the therapy over the six-month observation period (19). The observed safety profile suggested that biologic therapy could be integrated into routine practice without substantial compromise to patient safety, a crucial consideration for widespread adoption in populations with severe asthma who are already vulnerable to immunologic perturbations.

The study benefited from a randomized controlled design, ensuring balanced baseline characteristics and minimizing confounding effects (20). The high retention rate and adherence to follow-up visits strengthened the internal validity of the findings. Employing objective measures such as spirometry alongside validated patient-reported outcomes allowed for comprehensive assessment of both physiological and experiential aspects of asthma control. Conducting the study in the Urban Region Sindh provided practical insights into therapy performance within a high-density, industrially impacted population, enhancing the relevance of the results to similar real-world settings (21).

Several limitations were noted. The relatively short follow-up duration of six months, while sufficient to detect early improvements, restricted assessment of long-term durability of response and potential delayed adverse events. The sample size, though adequate for detecting differences in primary outcomes, limited the ability to explore rare safety events and subgroup analyses based on phenotype or comorbidities (22). The study setting, focused on a single urban region, may constrain generalizability to rural or less industrialized populations, where environmental triggers and healthcare access differ. Additionally, while adherence to therapy and follow-up was high, reliance on self-reported symptom diaries and telephone follow-ups for exacerbation recording could introduce reporting bias (23).

The findings highlighted the potential of biologic therapy to transform severe asthma management, providing robust reductions in exacerbation burden, improved lung function, and meaningful steroid-sparing benefits. Future research should aim for multicenter studies with larger and more diverse populations, extended follow-up durations, and mechanistic analyses to elucidate differential responses among asthma phenotypes. Comparative studies evaluating cost-effectiveness, long-term safety, and patient-centered outcomes would further support integration into routine clinical practice. Collectively, the study emphasized the clinical and therapeutic promise of biologic interventions while underscoring the need for ongoing evaluation to optimize their application in heterogeneous patient populations.

CONCLUSION

The study demonstrated that the new biologic therapy significantly reduced exacerbation frequency, improved lung function, enhanced symptom control, and enabled meaningful corticosteroid reduction in patients with severe asthma. The therapy was well-tolerated, with minimal adverse events, underscoring its safety in a high-risk population. These findings support the incorporation of targeted

biologic interventions as an effective strategy for optimizing disease control, minimizing systemic steroid exposure, and improving overall patient outcomes in routine clinical practice.

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