

**BIOLOGICALS IN SEVERE ASTHMA****Saurabh Karmakar<sup>1</sup>, Abdul Raouf Wani<sup>2</sup>, Vinay V<sup>3</sup>***Address for Correspondence: Department of Pulmonary Medicine, All India Institute of Medical Sciences, Patna, India.<sup>1,2,3</sup>*

Received:- 26/08/2023

Revised:- 30/08/2023

Accepted:- 10/09/2023

**INTRODUCTION**

Severe asthma presents a substantial challenge within the spectrum of asthma management, necessitating a comprehensive understanding of its complexities. Asthma, a chronic respiratory disorder characterized by airway inflammation and hyperresponsiveness, affects approximately 300 million individuals globally. While many manage their symptoms effectively, a subset grapples with persistent symptoms despite adhering to standard treatments, a condition known as severe asthma. This form of asthma diverges from milder variants due to its resistance to conventional therapies, often requiring high-dose medications or multiple therapies to maintain control. Despite these interventions, individuals with severe asthma frequently experience exacerbations, resulting in significant limitations in daily activities and impacting their quality of life. Understanding severe asthma necessitates recognizing its heterogeneous nature, influenced by diverse factors. Genetic predisposition, environmental triggers, and comorbidities such as allergic rhinitis, sinusitis, obesity, and psychological factors contribute to its severity. Additionally, specific biomarkers and phenotypes aid in identifying and managing severe asthma, guiding treatment decisions towards personalized therapies. Effective management of severe asthma requires a personalized approach tailored to each patient's unique circumstances. Multidisciplinary collaboration among respiratory specialists, allergists, immunologists, and pulmonologists is pivotal in crafting comprehensive treatment strategies. Advanced interventions such as biologic therapies targeting specific inflammatory pathways and bronchial thermoplasty have emerged as promising modalities. Patient education and support are integral components of

managing severe asthma. Educating patients about triggers, proper inhaler techniques, and self-management strategies empower them to better cope with their condition. Research and advancements in understanding severe asthma continually evolve, offering hope for improved treatments and outcomes. As the medical community delves deeper into its complexities, the overarching objective remains to mitigate the burden of severe asthma and enhance the lives of affected individuals.

**UNDERSTANDING BIOLOGICALS IN ASTHMA TREATMENT**

Biologicals, also known as biologics, are medications derived from living organisms or their components. In asthma management, biologicals specifically target key molecules and pathways involved in the inflammatory cascade, offering a more targeted and personalized approach.

- 1) Immunoglobulin E (IgE) Targeted Therapies: Monoclonal antibodies, such as omalizumab, bind to circulating IgE, reducing its interaction with mast cells and basophils, thereby mitigating allergic responses.
- 2) Interleukin-5 (IL-5) Inhibitors: Molecules like mepolizumab, benralizumab, and reslizumab target IL-5, a cytokine pivotal in eosinophilic asthma, reducing eosinophil levels and associated exacerbations.
- 3) IL-4 and IL-13 Blockers: Dupilumab, a monoclonal antibody, disrupts the IL-4 and IL-13 signalling pathway, crucial in type 2 inflammation, offering relief in severe asthma phenotypes. Patient Selection and Treatment Response Identifying Candidates

**PATIENT SELECTION AND TREATMENT RESPONSE IDENTIFYING CANDIDATES**

Patient selection involves a thorough assessment based on clinical and biological parameters. Phenotypic characterization, including identification of eosinophilic, allergic, or neutrophilic phenotypes, aids in selecting

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**How to cite this article:**

Karmakar S, Wani AR, Vinay V, Biologicals In Severe Asthma

suitable candidates for specific biological agents."Biomarkers such as blood eosinophil count, fractional exhaled nitric oxide (FeNO), and serum periostin levels assist in predicting response to targeted therapies, guiding personalized treatment choices. Patients experiencing severe, uncontrolled asthma despite adherence to high-dose inhaled corticosteroids and other controller medications are considered prime candidates for biological interventions.

#### **PREDICTING TREATMENT RESPONSE**

Monitoring treatment response involves various clinical markers. Improvement in symptoms, reduced exacerbations, and enhanced lung function signify positive treatment response.<sup>11</sup> Effective biological therapies often lead to reductions in biomarkers associated with asthma inflammation, such as decreased eosinophil counts or FeNO levels.<sup>12</sup> Enhanced quality of life, reduced rescue medication use, and decreased frequency of severe exacerbations indicate favourable treatment response.

#### **EFFICACY AND CLINICAL OUTCOMES**

Clinical trials, like the DREAM and MENSA studies, highlight the efficacy of mepolizumab in reducing exacerbations and improving lung function in patients with severe eosinophilic asthma,<sup>13</sup> Similarly, dupilumab, through its inhibition of IL-4 and IL-13, has exhibited reduced exacerbation rates, improved lung function, and enhanced quality of life for patients with severe asthma. Moreover, real-world studies have supported these findings, demonstrating the sustained effectiveness of these biologics in routine clinical practice, further solidifying their role in managing severe asthma and improving patient outcomes.<sup>15</sup> Adverse Effects Omalizumab, a monoclonal antibody targeting IgE, may lead to injection site reactions, viral infections, and in rare cases, anaphylaxis.<sup>16</sup> Mepolizumab and benralizumab, both targeting interleukin-5, have been linked to potential adverse effects such as hypersensitivity reactions, headache, and respiratory tract infections. Moreover, respiratory infections remain a concern with biologics, especially in individuals with compromised immune systems. These infections might include upper respiratory tract infections, sinusitis, and pneumonia, though the risk appears relatively low.<sup>18</sup> Cost-effectiveness and Accessibility Cost-effectiveness and accessibility of biologics in severe asthma are pivotal considerations in optimizing treatment strategies. Studies have shown that while these biologics, like omalizumab, mepolizumab, benralizumab, and

dupilumab, demonstrate efficacy in reducing exacerbations and improving lung function in severe asthma patients, their high costs create barriers to accessibility for many individuals. A substantial economic burden associated with these therapies, limiting access and affordability for a considerable proportion of patients.<sup>19</sup> Additionally, the cost-effectiveness of these biological agents has been a subject of debate. Assessing their value in terms of their clinical benefits against the incurred expenses is essential. Analysis of the cost-effectiveness of biological therapies in severe asthma reveals that while these treatments provide clinical benefits, their cost-effectiveness varies among different patient subgroups.<sup>20</sup> Strategies aimed at improving accessibility while ensuring cost-effectiveness involve the development of biosimilars and alternative reimbursement models. Biological therapies present promising avenues for severe asthma patients.

#### **CONCLUSION**

Remarkable advancements in biological treatments have ushered in a new era of hope for individuals grappling with severe asthma. These targeted therapies, alongside evolving combination approaches, have revolutionized disease management, offering tailored solutions and improved outcomes for patients resistant to conventional treatments. As research continues to delve deeper into understanding asthma's complex mechanisms, the future holds promise for even more precise and personalized biological interventions. The ongoing quest for novel targets, enhanced delivery systems, and a deeper comprehension of individualized treatment pathways underscores an optimistic horizon in the journey toward better controlling severe asthma and improving the quality of life for those affected

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