

Asthma Heterogeneity- An Update and Challenges

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Asthma is an obstructive pulmonary disorder affecting approximately 334 million people worldwide. It is known to affect both children and adults with enormous mortality and morbidity. Asthma is a non-communicable disorder; however, it has been documented that asthmatic patients are prone to infections and non-communicable chronic co-morbidities which further worsen the condition of these patients. Asthma puts a huge financial burden on patients, besides worsening their quality of their social life [1].

Though characterized by chronic airway inflammation, asthma is heterogenous, based on its clinical phenotypes and symptoms. This heterogeneity in asthma makes drugs and therapies discriminative. Diagnosis is an initial and essential criterion to circumvent the heterogeneity as an obstacle in treatment to some degree. Also, there is an overlap in clinical phenotype and symptoms of asthma with other acute or chronic lung disorders [2], which also makes diagnostic evaluation indispensable [3,4].

There are several clinical phenotypes of asthma which are based on its clinical and pathophysiological characteristics. These include allergic asthma, non-allergic asthma, asthma with persistent airflow limitation, adult-onset asthma, occupational asthma, and asthma-with- obesity. So, there are several layers of heterogeneity associated with asthma which make the therapeutic targets multicentric and multifactorial. However, patients of almost all asthma phenotypes respond to inhaled corticosteroid (ICS) treatment, which however is not a drug-class of choice, due to their side effects [3].

The 2019 update of The Global Initiative for Asthma (GINA) does not recommend the use of short-acting beta 2-agonists alone, which has been reported to increase the risk of exacerbations. Then broadly, there are three categories of available asthma treatments considering long-term use These include 1) Controller medications, which reduce the pathological inflammation associated with asthma and other associated symptoms like lung function. An example of this class is low dose ICS-formoterol. 2) Reliever (rescue) medications, which are consumed to deter all asthma-related symptoms and mostly prescribed if long term use is warranted. The ideal purpose of this class of medicine is to reduce the dependency of a patient on these medications or manage without it. 3) Add-on therapies for patients with severe asthma, which mainly include long-acting beta-agonists (LABAs). These are lifesaving drugs among all asthma medications. The commonly used LABAs include Salmeterol, Formoterol, and Arformoterol [3]. These are very effective drugs, though with several side effects. LABAs are also prescribed as combination therapy with ICS, making it more effective, though more toxic. There are several such combination medicines which include: Fluticasone/salmeterol, Budesonide/formoterol, Mometasone/formoterol, and Fluticasone/vilanterol. Discovery and identification of new small molecules or biological therapies for asthma is an ongoing process, which most often fail for not making it to the clinical level, due to lack of drug-like-properties in them such as a promising pharmacokinetic and pharmacodynamics profile [5-8].

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