

Editorial

Bronchial asthma - Issues for the developing world

Bronchial asthma is heterogeneous pulmonary disorder characterized by recurrent episodes of cough, breathlessness and wheezing, which may resolve spontaneously or after the use of bronchodilator medication¹. The global prevalence of asthma is anticipated to be approximately 4.5 per cent^{2,3}. There are about 334 million patients with asthma affecting all age groups, across the world⁴. The prevalence of asthma has increased over time and an additional 100 million people worldwide are expected to develop asthma by the year 2025⁴. In the Indian study on epidemiology of asthma, respiratory symptoms and chronic bronchitis in adults (INSEARCH), a survey conducted in two phases across 16 centers in India, the prevalence of asthma in adults was 2.05 per cent, with an estimated burden of 17.23 million⁵. A recent analysis using three different estimate models (INSEARCH, GINA and WHO survey) suggests that the prevalence of asthma in India varies between 2.05 to 3.5 per cent (17-30 million patients)⁶. The estimated cost of asthma treatment per year for the year 2015 has been calculated to be approximately ₹139.45 billion⁷. An estimated 15 million disability adjusted life years (DALYs) are lost due to asthma^{3,8}.

Although asthma is a major health problem in the world, there are some important issues, particularly its management. The real issues particularly in resource limited settings like ours are patient's lack of awareness about the disease, use of alternative forms of therapy without any proven efficacy or evidence, physicians not using step-wise practice guidelines in the management of patients, and most importantly inability to afford inhalers/medications because of the cost. It is internationally recommended that the management of asthma should follow a step-wise

standardized approach and dose/type of medication is adjusted accordingly to achieve complete symptom control and normal lung function. From the GINA (Global Initiative for Asthma) guidelines, International Union Against Tuberculosis and Lung disease produced an adapted version for low and middle-income settings. The Union uses low-cost essential medicines in its 4-step approach, with a package of technical measures for asthma management in the general health services. Implementing The Union's Asthma Guide has been shown in low and middle-income settings to reduce the severity of asthma for the majority of patients.

Physicians across India depend primarily on the International guidelines like the GINA guidelines to manage patients with asthma⁸. Although the international guidelines are evidence-based, it is important to realize that these may not be applicable to our population. A joint effort by Indian Chest Society/ National College of Chest Physicians has recently formulated evidence-based guidelines for management of bronchial asthma in adult Indian population, to better suit our country¹.

Asthma is a T-helper-2 (Th2)-cell-dependent, IgE-mediated allergic disease. Both non-modifiable (advancing age, female gender, history of atopy, polymorphism of GSTM1, GSTT 1, MBL2 and others) and modifiable (tobacco smoke, biomass smoke exposure, infections, occupation, diet and others)^{5,9,10} risk factors are considered to play a role in the development of asthma. Factors such as exposure to cold air, extreme emotional arousal, physical exercise, aspirin, beta-blockers, indoor allergens and others can precipitate asthma symptoms. Contrary to the prior belief, small airways are the major site of physiological airflow obstruction in asthma. Structural changes such

as goblet cell hyperplasia, airway smooth muscle hyperplasia and hypertrophy, along with subepithelial fibrosis are the hallmark of asthma and can be present even in mild disease.

The goals of asthma management include relief of patient's current symptoms and prevention of further disease progression. The patient should be able to carry out all his/her routine activities without any functional impairment. Many physicians in India still use short acting β_2 agonist (SABA) for treating asthma. This approach does not control airway inflammation and can cause progression of airway obstruction and remodelling. To achieve control of symptoms and prevention of remodelling, inhaled corticosteroids (ICS) should be used as the preferred form of therapy. However, further trials are needed to recommend such a strategy routinely in patients with mild asthma¹¹⁻¹³. In patients with poorly controlled asthma despite low to moderate doses of ICS, adding long-acting β_2 agonist (LABA) to ICS significantly reduces the risk of exacerbations and improves asthma control, when compared to increasing the dose of ICS¹⁴⁻¹⁶. The combination of ICS/LABA is also superior to ICS/methylxanthine combination and ICS/leukotriene receptor antagonist (LTRA) combination¹⁷.

In asthmatics who remain symptomatic despite high dose ICS and/or oral corticosteroids, treatment with omalizumab, mepolizumab, and lebrikizumab has been tried. Omalizumab is a monoclonal antibody (mAb) directed against IgE and has been shown to reduce the number of asthma exacerbations, and results in reduction or withdrawal of inhaled/oral corticosteroids^{18,19}. Omalizumab needs to be given for at least 24 weeks (some advocate indefinite therapy) to achieve therapeutic benefit. The use of omalizumab may not be practical in our country because of its high cost. A meta-analysis in asthmatic patients found the use of mepolizumab, a monoclonal antibody that acts against interleukin (IL)-5, to reduce the risk of asthma exacerbations and improve the quality of life. However, the use of mepolizumab did not lead to improvement in lung function²⁰. The use of lebrikizumab, another mAb that acts against IL-13, was associated with improvement in lung function in patients with high serum periostin levels. However, there was no difference in the asthma symptom scores, use of rescue medications and number of exacerbations between the treatment and the control group²¹.

In patients with mild to moderate asthma with evidence of allergy to one or a few antigens, the use

of subcutaneous immunotherapy (SCIT) with a single allergen extract decreases asthma symptoms, and medication use²². The evidence supporting the use of sublingual immunotherapy is rather weak; it does not lead to improvement in symptoms scores or reduction in medication use when compared to placebo²³.

Patients with asthma are prone to complications such as airway remodelling, bronchiectasis, allergic bronchopulmonary aspergillosis (ABPA), and others. ABPA is an allergic pulmonary disorder caused by immune responses to inhaled *Aspergillus fumigatus* spores, manifesting itself from poorly controlled asthma to structural lung damage (fibrosis, bronchiectasis and others) and finally respiratory failure and cor pulmonale, and hence should be screened for, especially in patients with poorly controlled asthma²⁴.

In conclusion, treatment of asthma involves identification and avoidance of precipitating agents and addition of medication in a step-wise manner. Inhaled corticosteroids are recognized as the cornerstone of management of patients with asthma.

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