Review Article

Challenges with Present Symptom Control and Risk Reduction of Future Exacerbations in Asthma: Indian Patients' Perspectives

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Abstract

Asthma poses a serious burden and remains poorly understood and unrecognized, in lower- and middle-income countries such as India where healthcare resources are already constrained. Several misconceptions exist among Indian patients regarding asthma, including the nature of the disease. Poor adherence to maintenance treatment leads to inadequate control of underlying inflammation which, in turn, increases the chances of subsequent exacerbations. Effective management of asthma should aim to control symptoms, decrease risk of exacerbations, and minimize fixed airflow limitation and side effects. Patient education and counseling also play a key role. A control-based management of asthma is recommended with the adjustment of medications via a stepwise approach. A single inhaler for both maintenance and reliever therapy offers an approach that can provide rapid relief, simplify asthma therapy, and prevent asthma exacerbations, while decreasing the total corticosteroid dose taken over time. For this review, a literature search was conducted using PubMed and other library searches to collate data on the Indian patients' perspectives on the level of asthma control and the associated risk of asthma exacerbations. We discuss the perceptions among Indian asthma patients regarding the disease, the gaps in asthma management, the key aspects of Global Initiative for Asthma Guidelines, and the role of single inhaler for both maintenance and reliever therapy in the management of asthma.

Keywords: Global Initiative for Asthma, maintenance, single inhaler

Introduction

Around 334 million people in the world suffer from asthma.[1] The World Health Organization estimated that 15–20 million individuals in India suffer from asthma.[2] The World Health Survey reported an overall prevalence of clinical asthma in Indian adults as 3.3%,[3] ranging from 2.05% to 7.5% across Indian studies.[4-7] In 2015, about 0.40 million people died from asthma, a decrease of 26.7% from 1990, and the age-standardized death rate decreased by 58.8%. The prevalence of asthma increased by 12.6%, while the age-standardized prevalence decreased by 17.7%.[8]

Globally, the number of disability-adjusted life years lost due to asthma was estimated to be 26.2 million, which represented 1.1% of global burden in 2015.[8] The Asia Pacific – Asthma Insights and Management Survey conducted in eight urban cities in India reported the presence of daytime symptoms daily or on most days in 31% of individuals and nighttime symptoms daily or on most nights in 15% of individuals with asthma. Troublesome symptoms were experienced by more than 60% of patients, which had a negative impact on their quality of life, and a significant proportion reported absenteeism leading to loss of productivity.[9]

The occurrence of exacerbations in Indian asthma patients has been found to be high, reflecting poor control of the disease, and a large proportion of patients overestimate their level of control. Nearly 50% of patients with asthma reported 3–10

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exacerbations per year and 20% experienced more than 11 exacerbations per year. An average of 8.4 exacerbations per year have been reported in India, with each episode lasting for about an average of 4 days.[9,10]

In low- and middle-income countries with underprivileged and fragile healthcare settings, asthma poses a serious burden. The economic burden of asthma is significantly high with indirect costs (loss of productivity), contributing as much to the economic loss as direct costs.[1] In this review, we review the latest literature using PubMed and library searches on the perceptions of Indian patients about asthma, the gaps in its management, the salient aspects of international guidelines, and the role of single inhaler for maintenance and reliever treatment of asthma.

Perceptions about Asthma in India

In India, the majority of patients with asthma were less informed about the etiology, pathophysiology, and treatment of the condition.[11] The pathophysiology, precise symptoms, use of the prescribed medications, and the efficacy of steroids in the control of asthma still remain ambiguous to a considerable number of patients.[11] It was observed that children too failed to accept the disease due to social stigma attached to it.[12] A significant gap exists between the guidelines for asthma care and clinical practice in India.[11,13]

Inhalers

Oral medications are often preferred to inhalational therapy for the treatment of asthma in India.[14] Studies have found that a considerable number of patients were either not prescribed inhalers or did not use inhaled medications.[9,11,13,15] In many patients, the technique of using the inhalers was found to be incorrect.[14,16-19] Failure to shake the inhaler (where appropriate), press the button at the right time, hold the breath after completing inhalation, and exhale completely before inspiration were the mistakes being committed.[12] A number of patients reported that they had learned the technique of using an inhaler from paramedical staff or from instructions in the package inserts.[16,20] Inability of the healthcare professionals to show the proper technique and misunderstanding or lack of instruction were the reasons for discontinuing inhaler therapy.[14,16] Various cultural issues, belief that these devices were unsafe or addictive, costly, difficult to use, unproductive, and forgetfulness deter the use of inhalational devices.[12,14,21,22] Some patients stopped using inhaled steroids during the treatment because they are apprehensive about using steroids or they find it ineffective.[16]

Barthwal *et al*. noted that a large number of patients use a short-acting beta-agonist (SABA) regularly.[16] Inhaled corticosteroids (ICSs) were often found to be underused among Indian patients due to the belief that regular controller medications are not required for the management of asthma and due to fear of using steroids.[9,18] It was also noticed that drugs providing symptomatic relief were being prescribed more often than asthma controllers.[15]

The preference for metered-dose inhaler (MDI) or dry powder inhalers varied among patients in India. Using spacers along with MDIs reduces chances of developing oropharyngeal candidiasis and systemic side effects while taking ICSs.[16] However, the use of spacers was found to be infrequent among the patients.[16,19] Spacers have some limitations as they are bulky and difficult to carry around. At times, the valves can become faulty or can stick, thus hampering drug delivery.[23]

Peak flow meters

It has been found that in developing countries, physicians go by the symptoms of patients, rather than lung function tests, to assess the severity of asthma.[24] Even though the Global Initiative for Asthma (GINA) guidelines specify that lung function testing (using forced expiratory volume in 1 s or peak expiratory flow rate) is vital to assess the variation in airflow limitation, lung function tests were done in <20% of patients in several studies in India.[11,13,16,25] One study reported that only 10.5% of doctors owned a peak flow meter for diagnostic purposes.[26] Only a minority of patients were aware of the fact that severity of an asthmatic attack could be assessed using a peak flow meter.[11]

Role of doctors in the management of asthma

The knowledge of doctors in India regarding asthma management seems to be inadequate. A majority of patients with asthma either remain undiagnosed or are wrongly diagnosed. Among those diagnosed, many do not receive adequate treatment or are poorly treated.[9] Physicians do not follow stepwise management recommendations of asthma. A significant proportion still prescribe only SABA for asthma treatment, which fails to address the underlying inflammation resulting in disease progression.[27]

A large number of patients are not being provided with a written plan to manage an acute attack of asthma. Even among those who do receive a written plan, there is a lack of communication from the doctor regarding the plan and importance to the patient.[11]

In a study conducted in an urban Indian community, the quality of asthma management was found to be unsatisfactory. The asthma management followed by general practitioners did not comply with the recommended treatment guidelines. A spirometer or peak flow meter was used in only 10% and 18% of patients, respectively, for making the diagnosis. Only 44% of patients in the study were prescribed inhalers by their treating doctors.[11] Bhattacharyya *et al*. observed a wide gap between the practice behavior of doctors and the established guidelines for asthma therapy, irrespective of the level of qualification of doctors. The practice of using spirometry or pulmonary function tests for evaluating a patient was found to be extremely low among all levels of doctors.[13]

It is essential that doctors keep themselves up-to-date regarding the latest evidence-based treatments for asthma.

Role of patient education

Gupta and Gupta observed a better adherence to treatment and use of inhalers in patients who visited specialist doctors or

who were treated at a medical institute compared with patients attended by general practitioners or unqualified practitioners.[22]

An increase in the awareness and education of patients about asthma is necessary for the effective management of asthma. Patients are generally not educated about the disease pathophysiology, and few patients are told how to manage an exacerbation.[20] Salvi *et al*. observed that patients with asthma in India who claimed that their disease was partly controlled or uncontrolled were not so as per the GINA guidelines.[9] There is a large gap between the actual and "patient-perceived" control of asthma among patients in India. Sixty percent of patients felt that their asthma was somewhat controlled while only 2% felt that it is completely controlled. The proportion of patients who felt their asthma to be well controlled, poorly controlled and uncontrolled were 29%, 7% and 2% respectively.[9] But according to the criteria of GINA guidelines 60% of these patients were partly controlled, 40% were uncontrolled and none were well controlled.[9] Patients tend to assume that suffering is a part of the disease, and they learn to tolerate the symptoms associated with asthma.

Patients need to be instructed that they should not ignore the symptoms of asthma, and appropriate treatment including the use of inhalational therapy is necessary to address the morbidity associated with the disease.[9] The majority of patients in India are frequently unaware of reasons for prescription of inhalers and the medicine dispensed.[11] The optimal asthma education program ensures better adherence with treatment, improvement in symptoms, and reduction in limitation of activity, thereby enhancing the quality of life of individuals with asthma.[18] Patient education must be reinforced with a written self-management plan to achieve sustained control of asthma.[20]

Treating to Control Current Symptoms and Minimize Future Risk of Exacerbations

Diagnosing asthma at the initial presentation itself is important because treatment may mask the characteristic signs and symptoms of asthma, thereby making it difficult to confirm the diagnosis later on. Assessing whether a patient's asthma is controlled consists of estimating whether the symptoms are under control and estimating a future risk of developing negative outcomes as well as assessing issues with prescribed treatment. Poor control of symptoms increases the risk of developing exacerbations. However, if risk factors such as smoking, history of ≥1 exacerbation in the previous year, blood eosinophilia, low lung function, incorrect inhaler technique, and poor adherence are present, then exacerbations may occur despite having symptom control. Use of sham treatments, placebos, short SABAs, or long-acting beta-agonists (LABAs) alone may relieve the symptoms of asthma but does not treat the underlying airway inflammation.[25]

The GINA guidelines classify asthma symptom control into well controlled, partly controlled, and uncontrolled based on four parameters: presence of daytime symptoms more than twice per week, nocturnal awakening due to symptoms, need for rescue medications, and limitation of activities. The risk factors need to be assessed at the time of diagnosis and periodically thereafter. Lung function has to be measured at the commencement of treatment and after undergoing controller treatment for 3–6 months. Lung function tests should be done at periodic intervals for future risk assessment. Presence of characteristic symptoms and demonstration of variable airflow limitation constitute the criteria for arriving at a diagnosis of asthma. Variable airflow limitation may be assessed by monitoring lung function after 4 weeks of anti-inflammatory treatment, bronchodilator reversibility test, peak expiratory flow variability, exercise challenge test, and bronchial challenge test.[25]

Bateman *et al*. developed a simple "risk score for exacerbations" for identifying patients with asthma who require treatment to reduce the risk of exacerbations and for comparing the efficacy of different treatments in improving the risk of exacerbations across a range of risk categories. It was found that the GINA step at diagnosis, postbronchodilator forced expiratory volume in 1 s, mean daily reliever use, and the Asthma Control Questionnaire-5 (ACQ-5) score were the good predictors of risk of exacerbations. Asthma symptom scores and smoking status could also predict the risk of developing uncontrolled asthma, and body mass index could portend severe exacerbation.[28]

The GINA guidelines state that asthma management should be able to effectively control symptoms, reduce risk of exacerbations, minimize side effects, and minimize fixed airflow limitation. A control-based management is advised, where a continuous cycle of assessment, treatment, and review of the patient's response occurs.

A stepwise concept is recommended for the treatment of asthma. Controller medications are used for maintenance treatment on a regular basis, and rescue or reliever medications are used at the time of exacerbations or worsening of asthma. Adjustment of controller medications is done in a stepwise approach, and after good asthma control has been achieved for 2–3 months, the minimum effective treatment can be determined by gradually stepping down the treatment.[25]

In step 1, GINA advises use of inhaled SABAs as needed in patients with daytime symptoms less than twice per month of short duration, no nocturnal awakening, absence of risk factors for exacerbations, and normal lung function. Once the symptoms surpass this level, a low-dose ICS may be added that can improve quality of life, increase lung function, and lower the possibility of exacerbations. A SABA is supplemented with one or two controller medications in step 3 and two or more controllers in step 4. Step 5 calls for referral to a specialist and add-on treatment with drugs such as tiotropium, immunomodulators, and low-dose oral corticosteroids as well as bronchial thermoplasty.[25] Combination low-dose ICS/formoterol can be used as single inhaler maintenance and reliever therapy from steps 3–5.[29]

Before considering a step-up in treatment, it is necessary to confirm that the symptoms are due to asthma and to check for environmental exposure, incorrect inhaler technique, and poor adherence.[25]

Role of Single Inhaler for Both Maintenance and Reliever Therapy in the Management of Asthma

According to the GINA recommendations, a LABA may be added as a step-up in adults on an ICS with uncontrolled asthma.[25] The use of a single inhaler for both maintenance and reliever therapy was found to achieve adequate asthma control and reduce exacerbations in patients with uncontrolled disease as well as in patients with mild-to-moderate asthma.[30,31] In the single inhaler for both maintenance and reliever therapy approach, a combination of formoterol and budesonide is dispensed from a single inhaler.[32,33]

The standard dose for maintenance and reliever therapy with budesonide/formoterol is 160/4.5 μg, one inhalation twice daily.[34] The patients may use a low dose of the budesonide/formoterol combination when asthma is controlled and may temporarily increase the dose for 1–2 weeks during an exacerbation.[35] Formoterol is a fast-acting LABA that provides rapid symptom relief, while budesonide has an anti-inflammatory effect.[30] The use of reliever medication such as SABA is reduced with this approach, and at the time of asthma worsening, the steroid dose can be increased by temporarily quadrupling the maintenance dose.[33,35]

Single inhaler for both maintenance and reliever therapy is able to prevent and reduce frequency of exacerbations and worsening of asthma, while decreasing the total corticosteroid dose taken over time and at a lower cost.[33,35-40] The time to first severe exacerbation was prolonged in patients using this approach as compared to those using conventional best practice, which was not statistically significant. These patients experienced 15% fewer exacerbations and 28% lower total number of days with exacerbations which were significant.[37]

Poor adherence can lead to underuse of ICS, resulting in ineffective management. The use of a single inhaler containing budesonide and formoterol for both maintenance and symptom relief in poorly adherent patients almost doubled the dose of budesonide taken, thus overcoming the problem of underuse of ICS.[32] The use of single inhaler for both maintenance and reliever therapy improves adherence in patients with asthma as it simplifies the treatment regimen and is more convenient.[35] This approach can compensate for any lack of patient education as well as miscommunication.[29]

The SMARTASIA study investigated the effect of using budesonide/formoterol therapy as both maintenance and reliever therapy in patients across Asia. One hundred and sixty-two patients from India were included in this study. A significant improvement in the ACQ-5 score was observed as early as 4 weeks from the start of therapy. A considerable improvement in the control of asthma and quality of life was seen among the patients from India. Patients reported a decrease in sleep disturbances and an increase in symptom-free days and lung function. There was significant reduction in the number of inhalations of as-needed reliever medications for night- and day-time and increase in as-needed medication-free days.[41] This is in concordance with other studies from India.[42,43]

Single inhaler for both maintenance and reliever therapy has been recommended in the GINA guidelines, the British Thoracic Society/Scottish Intercollegiate Guidelines Network Asthma Guidelines, and the Guidelines for Diagnosis and Management of Bronchial Asthma by the Indian Chest Society and the National College of Chest Physicians of India.[25,44,45]

Conclusion

In India, a large number of patients with asthma are unaware about the disease, pathophysiology, precise symptoms, and use of the prescribed medications. A significant gap exists between the guidelines for the management of asthma and what is being practiced in clinical settings. There is also a large gap between the guideline-based control and "patient-perceived" control of asthma among patients in India. A considerable number of patients do not use inhaled medications, and the technique of using inhalers has been found to be incorrect in many patients. Patient education is essential to achieve optimum management of asthma. A single inhaler for both maintenance and reliever therapy, consisting of formoterol and ICSs such as budesonide or beclomethasone, can ensure patient adherence to treatment while providing rapid symptom relief and reduce frequency of exacerbations. It prevents exacerbations by providing an earlier step-up in controller therapy during the window of opportunity when symptoms worsen. It can help overcome poor adherence to ICS that is generally seen among Indian patients. This approach reduces the need for reliever medications (i.e., SABA) and can allow increase in steroid dose during asthma worsening. It decreases the mean corticosteroid dose taken over time and is cost-effective. Thus, single inhaler for both maintenance and reliever therapy offers a simple, convenient, and effective approach to administer drugs.

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Conflicts of interest

Nila Velayudhan is an employee of AstraZeneca Pharma India Ltd., Bengaluru.

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