

Asthma - an update

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Abstract

Asthma is a common medical problem throughout the world. In spite of development in the therapeutic options, its prevalence has been increasing worldwide. With the increased understanding of the role of inflammation in asthma, greater stress has been laid on the early initiation of the anti-inflammatory therapy in the management. The national asthma education and prevention programme (NAEPP) have classified asthma according to severity of symptoms. They have also recommended a stepwise therapy according to clinical severity. Inhaled corticosteroids remain the main stay of therapy with a short acting beta 2 agonist used as needed for symptom relief.

Keywords: Asthma; management.

Introduction

Although asthma has always been a common medical problem, its prevalence has increased worldwide over the past 29 years. Much research has been done in this field, which has redefined asthma. To help health care professionals bridge the gap between current knowledge and practice, the National Asthma Education and Prevention Program (NAEPP) has convened two expert panels to prepare guidelines for the diagnosis and management.^{1,2}

Pathogenesis and definition

Asthma was long defined as reversible obstructive airway disease caused by abnormal control of the airway smooth muscle. Recent studies of asthma pathophysiology, including direct sampling of lower airway cells or the secretions by flexible bronchoscopy, have changed the concept to a disease of chronic inflammation and airway hyperresponsiveness.³ The principal pathologic finding in asthma is infiltration of the lower respiratory mucosa and secretions with inflammatory cells.³ The principal pathologic finding in asthma is the infiltration of the lower respiratory mucosa and secretions with inflammatory cells.⁴ Thus asthma is now defined as a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role, in particular, mast cells, eosinophils, T lymphocytes, neutrophils, and epithelial cells. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and cough, particularly at night and in the early morning.¹ These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment. The inflammation also causes an associated increase in the existing bronchial hyperresponsiveness (increased susceptibility to bronchoconstriction) to a variety of stimuli. Chronic airway inflammation can lead to thickening of the basement membrane and deposition of collagen in the bronchial wall. These changes, which are probably irreversible, contribute to the chronic small airway obstruction in asthma.

Diagnosis

Making the correct diagnosis is extremely important. The diagnosis of asthma is usually made accurately, although the degree of diagnostic accuracy is probably patient-age dependent. Asthma diagnosis in young adults is usually not difficult, since there are few other conditions that mimic asthma. With increasing age, however, cardiovascular disease and other chronic lung disease are more common, and the differential diagnosis of episodic chest symptoms is more extensive. The finding of an irreversible component of airway obstruction in older asthmatics causes confusion with COPD. The probability of misdiagnosis of asthma is highest in the elderly, who have the same high asthma prevalence (4-7%) as younger adults.⁵ The diagnosis is based on the patients' medical history, physical examination and measurements of pulmonary function. One should determine that episodic symptoms of airflow obstruction are present, airflow obstruction is partially reversible and that alternate diagnoses are excluded. Cough, wheezing or dyspnea that worsen in the early morning hours are the typical complaints. Wheezing of the chest is one of the main characteristics of asthma, but because airway obstruction is erratic, examination of the chest during regular visits is often normal. It is important to note that wheezing may be absent even with moderate (up to 25% reduction in PEF) airway obstruction⁶, and during severe exacerbations of asthma when airflow is severely limited. Spirometry should be done as an initial assessment of patients with asthma.

Measurement that suggest obstruction of the small airways include:^{1,2}

reduction in Fev 1

reduction in PEF

reduction in ratio of Fev 1/FVC

reduction in mid expiratory flow rate (FEV 25-75)

For patients with evidence of airway obstruction, reversibility should be tested by administering Salbutamol either with a metered dose inhaler (MDI) and a spacer, or via nebulizer, and then PFT's should be repeated 15-30 minutes later. An increase in PEF or Fev1 of more than 12% from baseline values strongly supports the diagnosis of asthma.⁷ Some patients with asthma however, have subnormal responses to bronchodilator administration and this may be related to airway oedema and inflammation. In these patients, a short course (1-3 weeks) of oral corticosteroids (20 mg po BID) will produce significant improvement in pulmonary function if asthma exists.

Management of Asthma

Goals of therapy

1. Prevent chronic and troublesome symptoms of asthma.
2. Maintain (near) normal pulmonary function.
3. Maintain normal activity levels (including exercise and other physical activity)
4. Prevent recurrent exacerbations of asthma and minimize the need for hospitalizations.
5. Provide optimal pharmacotherapy with minimal or no adverse effects.

Asthma therapy includes several different components, including control of environmental triggers of asthma, use of antiinflammatory medications and bronchodilators, immunomodulation and patient education. This article will only discuss the aspects of drug therapy.

Classification of asthma

For many years asthma has been classified as extrinsic or intrinsic, depending on the suspected role of allergens as etiologic factors. By convention, atopic subjects are considered to have extrinsic asthma, while non atopic subjects have intrinsic asthma. This nomenclature lacks sufficient discriminative power to aid in establishing an etiologic diagnosis or to help in defining treatment strategies. The presence of atopy does not, by itself indicate that allergens are important triggers of asthma, since a large percentage of atopic persons report no asthma. Exercise and viral respiratory infections may play a more prominent role than allergens as triggers of symptoms in some atopic subjects.

The expert Panel Report (EPR) has changed the asthma severity from mild, moderate and severe to mild intermittent, mild persistent, moderate persistent and severe persistent which more accurately reflects the clinical manifestation of asthma. The patients at any level however, can have mild, moderate or severe exacerbations. In 1997 NAEPP report recommended a "step care" approach to asthma therapy. There are two appropriate approaches to initiating therapy for asthma. One approach is to start therapy at the level consistent with the severity of the patient's disease and increased treatment in steps if control is not obtained. The second approach (more aggressive) is to initiate therapy at a higher step than the patient's current level of disease severity and gradually "step down" once a control is obtained. Because asthma is a highly variable disease, the physician needs to individualise treatment strategies regularly follow-up visits are necessary to insure that good control is maintained and to evaluate the need for a step up or a step down in therapy.

Mild Intermittent

Patients in this category have symptoms less than twice a week. Night symptoms are less than twice a month. They are asymptomatic with normal PFT between exacerbations. The exacerbations are brief (few hours to few days), however the intensity may vary.

Mild Persistent

These patients have symptoms more than twice a week but less than once a day. Night symptoms are more than twice a month. Exacerbations may affect activity.

Moderate Persistent

Patients have daily symptoms with night symptoms more than once a week. Exacerbations are more than twice a week and affect activity.

Severe Persistent

Patients have continual symptoms with frequent exacerbations. They have frequent night symptoms and limited physical activity.

Daily long-term therapy is required for persistent asthma in addition to appropriate medication to manage acute exacerbations. The EPR-2 now categorizes medication into two general classes: Long-term control medications (controllers) to achieve and maintain control of persistent asthma and quick-relief medications (relievers) to treat symptoms and exacerbations. Because inflammation is considered an early and persistent component of asthma, therapy for persistent asthma must be directed toward long-term suppression of the inflammation. The most effective medications for long term control are those shown to have anti-inflammatory effects . Early intervention with inhaled corticosteroids can improve asthma control and normalize lung function.

Key points of management

1. Gain control as quickly as possible; then decrease treatment to the least medication necessary to maintain control.
2. A rescue course of systematic corticosteroids maybe needed at any time and at any step.
3. Some patients with intermittent asthma experience severe life threatening exacerbations separated by long periods of normal lung function and no symptoms. This maybe especially common with exacerbations provoked by respiratory infections. A short course of corticosteroids is recommended.

Treatment Protocol

Mild Intermitent Asthma (Step 1)

- No daily medication needed for long term control.
- Short acting bronchodilators (inhaled beta 2 agonist) should be used as needed for symptom relief.
- Use of short acting beta 2 agonist more than twice a week may indicate the need to initiate long term control therapy.

Mild Persistent Asthma (Step 2)

- Anti-inflammatory drugs should be the main stay of therapy.
- Either inhaled corticosteroids (low dose) or cromolyn or nedocromil.
- Alternatives are sustained released theophylline or zafirlukast or zileuton (patients above 12 years).
- Short acting beta 2 agonist as needed for symptom relief.

Moderate Persistent Asthma (Step 3)

- Medium dose inhaled corticosteroid.

or

- Low-medium dose inhaled corticoste-roids plus long acting brochodilators for night time symptoms (salmeterol or sustained released theophylline).

Severe Persistent Asthma (Step 4)

- High dose inhaled corticosteroids and long acting bronchodilators and oral corticosteroids daily dose not exceeding 60 mg.

Individual drugs

Corticosteroids

Most potent and effective anti-inflammatory medication currently available. Inhaled form is used in the long-term control of asthma. Systemic corticosteroids are used in long-term therapy to gain prompt control (rescue) of the disease and also to manage severe persistent asthma. Parenteral administration requires >6-24 hours to improve pulmonary function, thus its use in the emergency department (as is currently practised) does not relieve immediate symptoms.

Cromolyn sodium and nedocromil

Mild to moderate anti-inflammatory medications. In children, it is often used initially for persistent asthma because of their excellent safety records. Can also be used as preventive treatment prior to exercise, or to unavoidable exposure to known allergens. Provides effective prophylaxis for 1-2 hours.

Short acting beta-2 agonists

Therapy of choice for relief of acute symptoms and prevention of exercise bronchospasm (EIB). Regular long-term use is not recommended.

Long acting beta-2 agonists

Long acting bronchodilator used concomitantly with anti-inflammatory medications for long-term control of symptoms, especially nocturnal symptoms. Not to be used to treat acute symptoms or exacerbations. Also prevent EIB.

Methylxanthines

Sustained released theophylline is a mild to moderate bronchodilator used principally as adjuvant to inhaled corticosteroids for prevention of nocturnal asthma symptoms. May have mild anti-inflammatory effect. Theophylline has also been suggested to have various other respiratory effects, including reduced gas trapping, improved respiratory muscle function and gas exchange, and enhanced mucociliary clearance.⁹

Leukotriene modifiers

Zafirlukast, a leukotriene receptor antagonist, or Zileutin, a 5-lipoxygenase inhibitor, constitute a new class of medications that produce long-lasting bronchodilation, and also reduce blood eosinophil counts and antigen-induced eosinophil recruitment maybe considered alternative therapy to low doses of inhaled corticosteroids or cromolyn or nedocromil in the control of mild persistent asthma in patients >12 years of age.

Anticholinergics

Ipratropium bromide may provide some additive benefit to inhaled beta-2 agonists in severe exacerbations. It may be an alternative bronchodilator for patients who do not tolerate inhaled beta-2 agonists.

Conclusion

There has been a significant change in the understanding and management of asthma in the past decade. Asthma, is now considered a chronic inflammatory disease like Rheumatoid Arthritis. The recent change in severity classification has helped the management aspects. However, as asthma is characterized by considerable heterogeneity with respect to etiology, clinical presentation, severity, natural history, and response to therapy, treatment should be tailored to the individual patient. Inhalation route of therapy should be encouraged and inhalation Steroids remains the mainstay of pharmacological treatment for patients with persistent symptoms. Equally important are the nonpharmacological management aspects, including patient education and avoidance of asthma triggers.

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