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Review Article

Asthma: An Overview of Diagnosis and Management

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Abstract

Introduction: Asthma is a diverse chronic clinical illness that causes inflammation and airway constriction and primarily affects the lower respiratory tract and is characterized by wheezing, dyspnea, and coughing that may be episodic or ongoing. It frequently manifests in childhood and is frequently accompanied by ailments like eczema and hay fever. This activity describes the diagnosis, management, and involvement of the interprofessional team in the care of patients with asthma. These signs and the spirometry-based proof of reversible airway blockage are necessary for the diagnosis of asthma. It is helpful to identify allergy sensitivities that are clinically significant. While daily inhaled corticosteroids are the gold standard of therapy for persistent asthma, inhaled short-acting 2-agonists can quickly relieve acute symptoms. For patients for whom inhaled corticosteroids alone are not sufficient, combination therapy with long-acting 2-agonists is useful. Inhaled long-acting 2-agonists should not be used exclusively. Long-acting muscarinic antagonists (such as tiotropium) and biological medicines that target proteins involved in the etiology of asthma are further controller strategies (e.g. omalizumab, mepolizumab, reslizumab).

Aim of the Study: The purpose of the literature review is to understand various investigations, differential diagnoses, and treatments of asthma.

Methodology: The present study is a comprehensive research of PUBMED since the year 2011 to 2022.

Conclusion: Variable airway obstruction, airway hyperresponsiveness, and airway inflammation are hallmarks of asthma. Avoiding aggravating environmental factors, having access to short-acting 2-agonists for quick symptom relief, and using inhaled corticosteroids on a daily basis are all necessary for the management of chronic asthma. In cases of moderate and severe asthma, additional controller drugs, such as long-acting bronchodilators and biologics, can be needed. In general, patients with severe asthma benefit from speaking with an asthma expert to discuss possible additional treatments, such as injectable biologics.

Keywords: *Asthma; Airway Obstruction; Wheezing; Bronchodilators; Chest X-Ray*

Introduction

Asthma is one of the most prevalent chronic diseases in the world. It also has a significant financial impact on healthcare systems. For more than ten years, the Global Initiative for Asthma (GINA) has released annually revised guidelines for the diagnosis and treatment of asthma in children and adults. Based on a persistent bronchial inflammatory response, asthma is a diverse, multifaceted disease with varied and frequently reversible respiratory route blockage. A variety of symptoms, including cough, rhinitis, wheezing, chest tightness, and shortness of breath, are connected to expiratory flow restriction. Despite being frequently present, bronchial hyperresponsiveness (BHR) is no longer a required or sufficient diagnostic criterion according to the most recent GINA Guidelines [1].

Atopic vs. nonatopic asthma, aspirin-exacerbated respiratory illness, and obesity-associated asthma are only a few examples of the significant clinical and molecular variability that asthma presents. This complicates diagnostic evaluations and influences therapy responsiveness. Asthma patients who smoke, for instance, react relatively differently to inhaled corticosteroids. Patients with peripheral blood eosinophilia and uncontrolled asthma who are not responding to normal therapy may benefit from mepolizumab or reslizumab, and those with elevated levels of perennial allergen-specific IgE may be candidates for omalizumab. The evaluation of allergy sensitivities, spirometry, and clinical history are crucial for diagnosing asthma [2,3].

Phenotypes

Numerous different manifestations of the disease can be defined due to its variability. The therapy in difficult situations may benefit greatly from distinguishing between them [4]:

1. Late-onset asthma
2. Asthma with fixed airflow obstruction
3. Obesity asthma
4. Occupational asthma
5. Asthma in the elderly
6. Severe asthma
7. Allergic asthma
8. Nonallergic asthma
9. Pediatric asthma/recurrent obstructive bronchitis.

Other professional associations' classifications (such as those by the ERS/ATS, European Respiratory Society/American Thoracic Society, etc.) tend to place more emphasis on a combination of clinical and pathophysiological factors (such as those relating to eosinophilic/neutrophilic asthma, severe allergic asthma, etc.) [4].

Initial diagnosis

Initial evaluation Diagnostic standards and additional tests If the patient has a history of recurring dry coughing, particularly at night, rhonchus, wheezing, chest tightness, or shortness of breath, asthma may be considered. If an airway obstruction is discovered to be reversible based on an increase in FEV1 (Forced expiratory volume in 1 second) of > 12% and > 200 ml (in adults) following the administration of 200 - 400g salbutamol, lung function testing can confirm the diagnosis. Further bronchial challenge testing, such as with methacholine or indirect tests like running effort or inhaling hyperosmolar solutions, may be useful if there is clinical suspicion but normal lung function, particularly to identify adult bronchial hyperresponsiveness [5].

Additionally, following 4 weeks of anti-inflammatory medication, a rise in FEV1 of +12% and > 200 ml (in adults) is regarded as diagnostic confirmation. If an allergic trigger is thought to exist, a skin prick test, a definition of the specific IgE (immunoglobulin class E), and medical history should be used to make an allergy diagnosis. Sensitizations that are not clinically significant should also be included because they can offer prognostic information. The current guidelines for managing generalized asthma do not propose measuring fractional exhaled nitric oxide (FeNO) when making a decision about general therapy [6].

However, according to the authors of this statement, there are a number of situations in which a FeNO measurement makes sense, such as: (1) in cases where diagnosing asthma is challenging (normal lung function, ambiguous symptoms), (2) to monitor treatment compliance with inhaled corticosteroids (ICS), or (3) for the early detection of worsening asthma [6].

Final evaluation

Bedside

When determining the intensity of an asthma episode or keeping an eye out for deterioration, pulse oximetry can be helpful. It should be noted that pulse oximetry lags, and the physiological reserve of many patients makes a dropping pO_2 on pulse oximetry a late result, indicating a severely ill or peri-arrhythmic patient. Peak flow measurements can also be used to evaluate asthma, and they should always be compared to a nomogram and the patient's unique baseline function. Peak flow measurements are related to acute asthma attack severity and are expressed as a specified proportion of predicted peak flow [7].

Laboratory

If the patient takes a high dose or repeats salbutamol, urea and electrolytes (kidney function) should be taken since one of the salbutamol's adverse effects is a temporary shift of potassium into the intracellular space, which might result in temporary, iatrogenic hypokalemia. Eosinophilia is typical but not unique to asthma. Recent research suggests that sputum eosinophil counts may be used to direct treatment. Additionally, some patients may have elevated serum IgE levels. Respiratory acidosis and hypoxemia may be detected by arterial blood gas. Periostin may be a marker for asthma, according to studies, but its clinical significance is yet unknown. An ECG will show sinus tachycardia, which can be brought on by theophylline, albuterol or asthma [7].

Imaging

A chest x-ray is an important examination, particularly in individuals who have a history of infection or probable foreign body exposure. Patients with persistent symptoms who do not improve with treatment are given a chest CT scan [7].

Figure 1: *Showing chest-x ray for asthma [7].*

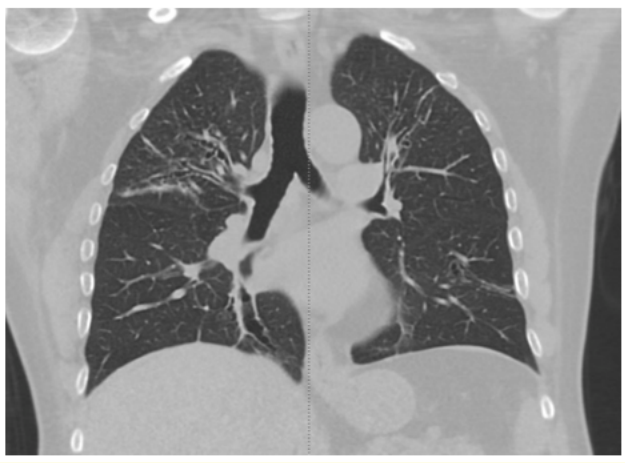

Figure 2: *Showing CT scan ray for asthma [7].*

Special tests

The preferred diagnostic technique is spirometry, which will reveal an obstructive pattern that is either entirely or partially relieved by salbutamol. In order to gauge the severity of the disease before starting treatment, spirometry should be performed. A reduced FEV1 to FVC ratio indicates airway obstruction, which is treatable and reversible. Short-acting beta 2 agonists are administered to the patient to do reversibility testing, and then the spirometry test is repeated. FEV1 improvement of 12%, or 200 ml, from the baseline, indicates reversibility and is diagnostic of bronchial asthma. Peak expiratory flow monitoring is widely used today and enables one to record therapeutic responses. This test's dependency on effort is a drawback. A methacholine/histamine challenge may be necessary for some patients to check for the presence of airway hyper-reactivity. Only experts with the necessary training should conduct this test. Activity spirometry may be used to detect those who have bronchoconstriction brought on by exercise [7].

Differential diagnosis

In addition to sinusitis or gastroesophageal reflux disease, the differential diagnosis for asthma in persons over 40 years of age should also include chronic obstructive pulmonary disease (COPD) (GERD). Since symptoms of COPD and asthma may overlap, fluctuate, or exist simultaneously, it can be challenging to distinguish between the two (ACOS Asthma COPD overlap syndrome). Acute infections, congenital cardiac or respiratory abnormalities, or foreign body aspirations may be more noticeable in younger patients [5]:

- Upper respiratory tract → Vocal cord dysfunction, Congestive rhinopathy, Obstructive sleep apnea syndrome.
- Lower respiratory tract→ Chronic obstructive pulmonary disease, Occupational bronchitis, Cystic fibrosis, Bronchiectasis Pneumonia.
- Gastrointestinal tract → Gastroesophageal reflux disease.
- Cardiovascular system → Congestive heart failure, Pulmonary hypertension, Chronic thromboembolic pulmonary disease.
- Central nervous system → Habitual cough.

Treatment

Asthma treatment aims to lessen symptoms, maintain daily activities, achieve [almost] normal lung function test results, and minimize dangers brought on by the condition (future exacerbations, medication adverse effects). Clinicians must approach patients with a guideline-based plan that recognizes specific environmental triggers and their mitigation (such as allergens, viruses, or irritants encountered in the occupational, household, or environmental settings), individual variability in the dose and particle size of inhaled corticosteroids, the class of long-acting bronchodilators, and the heterogeneous nature of asthma due to the limited availability of predictive biomarkers for treatment success [7].

Conservative approach

The patient should be calmed to encourage relaxation, moved outside or away from the likely allergen source, and cooled. It is occasionally practiced to take off clothing and wash the face and mouth to remove allergies, but this method lacks scientific support. Controlling the environment is essential to prevent recurrent assaults. Avoiding allergens can greatly enhance one's quality of life. This entails staying away from the pollen, dust mites, animals, and smoke. In obese asthmatics, losing weight improves control. Immunotherapy for allergies is still debatable. Large-scale research has yet to reveal any appreciable advantages, and the method is extremely expensive. For patients with moderate to severe asthma who have a positive skin test, monoclonal antibody therapy is advised. IgE levels may drop as a result of the therapy, which also impacts histamine production. The injections do come at a great price, though. A relatively new procedure called bronchial thermoplasty uses heat energy to treat the airway wall and lessen airway constriction. It can lessen emergency visits and days lost from school, according to numerous studies [8,9].

Control-based asthma management

The idea of asthma management is the foundation of contemporary asthma treatment (pharmacological and nonpharmacological therapy), which has been proven to increase the success of treatment. The cycle of assessment, adjustment, and review is the foundation of this idea. Asthma exacerbations are typically decreased when symptoms are under control. Sometimes, with more severe forms, symptom management does not coincide with a decreased exacerbation rate. Because of this, it's crucial to take into account both asthma control elements (symptoms and exacerbation risk). In rare circumstances, such as severe or challenging-to-treat asthma, other ideas, such as therapy based on sputum or FeNO, may be utilized as an alternative [5].

Medical management

Pharmacologic options are categorized as controller (longer-term benefit) or reliever (short-term benefit) drugs. A short-acting 2 agonist inhaler (commonly known as albuterol) should be available to all asthma patients for the treatment of acute symptoms; this in-

tervention alone is suitable for patients with intermittent asthma, which is defined as symptoms occurring less than twice weekly with (near) normal pulmonary function. A daily maintenance controller is typically recommended for people with chronic asthma, defined as symptoms occurring more than twice per week or abnormal pulmonary function. The classification of asthma severity (intermittent; mild; moderate; or severe persistent at diagnosis) guides the initial treatment choice. Standards in the United States prescribe treatment based on six phases; however, the GINA guidelines specify five steps [10]:

1. Step 1: Low-dose inhaled corticosteroids, and formoterol are the preferred controller when needed.
2. Step 2: Daily low-dose inhaled corticosteroids combined with need-based short-acting beta 2 agonists are the preferred controls.
3. Step 3: Low-dose inhaled corticosteroids, long-acting beta 2 agonists, and as-needed short-acting beta 2 agonists are the preferred controllers.
4. Step 4: A medium-dose inhaled corticosteroid, a long-acting beta 2 agonist, and short-acting beta 2 agonists as needed are the preferred controllers.
5. Step 5: Long-acting beta 2 agonist, high dose inhaled corticosteroid, and long-acting muscarinic antagonist/anti-IgE.

Patients with intermittent asthma receive step 1 therapy, which consists of short-acting 2-agonists that are given as needed. (These medications are also applied to all asthma sufferers, regardless of their level of illness) Low-dose inhaled corticosteroids are preferred for Step 2 therapy, which is appropriate for mild persistent asthma and improves exacerbations, symptoms, and lung function dose-dependently, but possibly not dose-proportionally (e.g. a doubled dose of inhaled corticosteroids will not produce doubled improvement in lung function). Depending on the outcome being examined, inhaled corticosteroids' dosage response varies (symptom reduction, lung function improvement, reduction in exacerbation). Eosinophil infiltration and activation, as well as that of TH2 cells and other inflammatory cells, are decreased by inhaled corticosteroids [11,12].

Starting step 3 therapy with medium-dose inhaled corticosteroids or a combination of low-dose inhaled corticosteroids and a long-acting 2 agonist is recommended for patients with moderate persistent asthma. For 12 to 24 hours, longer-acting bronchodilators widen the airways [11].

For patients with severe persistent asthma, which is typically indicated by near-constant chest symptoms, the requirement for multiple rescue 2 agonist inhalations per day, nightly awakenings due to asthma symptoms, or an FEV1 less than 60% predicted should begin at step 4, step 5, or step 6, and be referred for advice from an asthma specialist (an allergist or pulmonologist). Inhaled long-acting muscarinic agonists (tiotropium), inhaled medium- or high-dose inhaled corticosteroid plus long-acting 2 agonist combos, and biologic therapy is also possible treatment choices for these patients [13].

Once asthma has been effectively managed for two to three months, medication may be decreased to the lowest dose that still effectively manages symptoms and lung function. There are no randomized clinical trials of step-down therapy on which to base precise recommendations, and guidelines for deintensifying asthma therapy are not as well established as those for intensification [14].

Several parenteral biologic medicines (monoclonal antibodies) are available for patients whose uncontrolled asthma persists despite traditional inhalation therapy. Unlike traditional controller medicines, which address the effects of inflammation and bronchospasm from within the airway, these medications work systemically by altering the immunopathogenesis of asthma. IgE is a desirable target for the treatment of asthma because of its prominent role in the pathophysiology of allergic airway disease. Omalizumab, an anti-IgE monoclonal antibody, is utilized in allergic asthma when there is evidence of persistent aeroallergen sensitization as well as a moderately high IgE level (30 to roughly 1000 IU/mL, depending on body weight) [15].

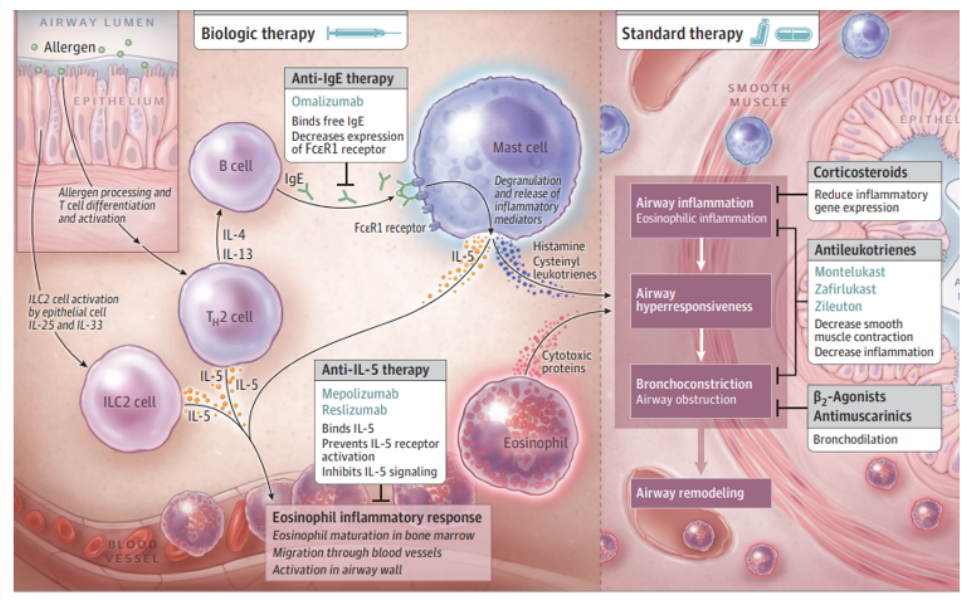

Figure 3: *Showing contrasting standard vs. biologic therapies in asthma [13].*

It decreases the activation of mast cells by allergens and the production of IgE high-affinity receptors on mast cells. Omalizumab is mostly beneficial in lowering exacerbations and the requirement for oral steroids. It is administered by subcutaneous injection every 2 to 4 weeks, with a dose and frequency based on body weight and blood IgE levels. According to a retrospective study of omalizumab trials, patients who had serum eosinophil counts above 260/L and fractional nitric oxide excretion levels at least 19.5 ppb may be identified as being likely to benefit from omalizumab. But no biomarker has been thoroughly prospectively confirmed to ascertain its prognostic usefulness [15].

Anti-IL-5 therapy may be useful in treating eosinophilic airway illness since interleukin 5 is crucial for the synthesis, maturation, homing, and activation of eosinophils. Recently released anti-IL-5 monoclonal antibodies include mepolizumab and reslizumab. With little impact on lung function, mepolizumab reduces the rate of exacerbations by approximately 50% and the need for oral corticosteroids by 50%. Reslizumab is given intravenously every 4 weeks using a weight-based dosage (3 mg/kg). Reslizumab lessens symptoms, cuts down on exacerbations by about 50%, and raises FEV1 by 110 mL [15].

Conclusion

Variable airway obstruction, airway hyperresponsiveness, and airway inflammation are hallmarks of asthma. Avoiding aggravating environmental factors, having access to short-acting 2-agonists for quick symptom relief, and using inhaled corticosteroids on a daily basis are all necessary for the management of chronic asthma. In cases of moderate and severe asthma, additional controller drugs, such as long-acting bronchodilators and biologics, can be needed. In general, patients with severe asthma benefit from speaking with an asthma expert to discuss possible additional treatments, such as injectable biologics.

Bibliography

1. Global Initiative for Asthma. Global Strategy for asthma management and prevention (2015).
2. Ray A., *et al*. "Emerging molecular phenotypes of asthma". *American Journal of Physiology-Lung Cellular and Molecular Physiology* 308.2 (2015): L130-L140.
3. Tripple JW., *et al*. "Biologic therapy in chronic obstructive pulmonary disease". *Immunology and Allergy Clinics* 37.2 (2017): 345-355.
4. McCracken JL., *et al*. "Diagnosis and management of asthma in adults: a review". *The Journal of the American Medical Association* 318.3 (2017): 279-290.
5. Horak F., *et al*. "Diagnosis and management of asthma–Statement on the 2015 GINA Guidelines". *Wiener Klinische Wochenschrift* 128.15 (2016): 541-554.
6. Pijnenburg MW., *et al*. "Monitoring asthma in children". *European Respiratory Journal* 45.4 (2015): 906-925.
7. Hashmi M F., *et al*. "Asthma". In Stat Pearls. Stat Pearls Publishing (2022).
8. Gosens R and Gross N. "The mode of action of anticholinergics in asthma". *European Respiratory Journal* 52.4 (2018).
9. Almadhoun K and Sharma S. "Bronchodilators". In Stat Pearls. Stat Pearls Publishing (2021).
10. Rajan S., *et al*. "The global initiative for asthma guidelines (2019): change in the recommendation for the management of mild asthma based on the SYGMA-2 trial–A critical appraisal". *Lung India: Official Organ of Indian Chest Society* 37.2 (2020): 169.
11. Szefler SJ., *et al*. "Management of asthma based on exhaled nitric oxide in addition to guideline-based treatment for inner-city adolescents and young adults: a randomised controlled trial". *The Lancet* 372.9643 (2008): 1065-1072.
12. Price D., *et al*. "Leukotriene antagonists as first-line or add-on asthma-controller therapy". *New England Journal of Medicine* 364.18 (2011): 1695-1707.
13. McCracken J., *et al*. "Biologic therapy in the management of asthma". *Current Opinion in Allergy and Clinical Immunology* 16.4 (2016): 375.
14. National Asthma Education, Prevention Program (National Heart, Lung, Blood Institute). Second Expert Panel on the Management of Asthma, National Heart, Lung, and Blood Institute. National Asthma Education Program. Expert Panel on the Management of Asthma. (1998). Expert panel report 2: guidelines for the diagnosis and management of asthma. National Institutes of Health, National Heart, Lung, and Blood Institute (1998).
15. Humbert M., *et al*. "Omalizumab in asthma: an update on recent developments". *The Journal of Allergy and Clinical Immunology: In Practice* 2.5 (2014): 525-536.
16. Busse W., *et al*. "Omalizumab, anti-IgE recombinant humanized monoclonal antibody, for the treatment of severe allergic asthma". *Journal of Allergy and Clinical Immunology* 108.2 (2001): 184-190.
17. Bel EH., *et al*. "Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma". *New England Journal of Medicine* 371.13 (2014): 1189-1197.
18. Ortega HG., *et al*. "Mepolizumab treatment in patients with severe eosinophilic asthma". *New England Journal of Medicine* 371.13 (2014): 1198-1207.

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