Asthma

Asthma: is a chronic inflammatory disorder of the airways causing airflow obstruction and recurrent episodes of wheezing, breathlessness, chest tightness, and coughing. The airflow obstruction is often reversible, either spontaneously or with treatment.

Epidemiology and Etiology

Current estimates suggest that asthma affects 300 million people worldwide, with a predicted additional 100 million people affected by 2025. The socio-economic impact is enormous, as poor control leads to days lost from school or work, and hospital admissions.

Asthma results from a complex interaction of genetic (the presence of asthma in a parent is a strong risk factor for development of asthma in a child) and environmental factors, but the underlying cause is not well understood. Although asthma can occur at any time. Most patients being diagnosed by 5 years of age.

Pathophysiology

Asthma is characterized by airway narrowing and inflammation. A key feature of the pathophysiology is airway hyperresponsiveness, which is exaggerated narrowing of the airways in response to a trigger or allergen such as cold air, strong odors, pollen, or dust. Airway narrowing results from contraction of airway smooth muscle, increased mucus secretion, airway edema, and remodeling.

Airway hyperresponsiveness (AHR) refers to the tendency of airways to narrow excessively in response to triggers that have little or no effect in normal individuals.

After exposure to an asthma-precipitating factors (Examples of these include inhaled allergens; respiratory viral infection; cold, dry air; smoke; other pollutants;…..), inflammatory mediators (such as histamine, leukotrienes, prostaglandins…) are released from the inflammatory cells (Mast cells, eosinophils, T lymphocytes) that cause airway injury, including mucus hypersecretion, airway edema , increased reactivity of smooth muscle and airway smooth muscle constriction resulting in airway obstruction.

Clinical Manifestations

a. Chronic asthma

Signs and Symptoms include episodes of dyspnea, chest tightness, dry, hacking cough (particularly at night), wheezing, or a whistling sound when breathing.

These often occur with exercise but may occur spontaneously or in association with known allergens.

b. Acute severe asthma

Patients may complain of severe dyspnea, shortness of breath, chest tightness, or burning. They may be able to say only a few words with each breath. Signs include expiratory and inspiratory wheezing on auscultation; dry, hacking cough; tachypnea; tachycardia; pallor or cyanosis; and hyperinflated chest with retractions. Patients may be anxious and agitated. Symptoms are unresponsive to usual measures [inhaled short-acting β-agonists (SABA)].

Diagnosis

The diagnosis of asthma is predominantly clinical and based on a characteristic history. History of recurrent episodes of coughing, wheezing, chest tightness, or shortness of breath. Patients may have family history of allergy or asthma or symptoms of allergic rhinitis.

Demonstration of airflow obstruction, preferably by using spirometry to measure forced expiratory volume in 1 second [FEV1] and forced vital capacity [FVC]. The FEV1 is a measure of the FEV in the first second of exhalation. The forced vital capacity (FVC) is the maximum volume of air exhaled with maximum effort after maximum inspiration.

The FEV1 usually is expressed as a percentage of the total volume of air exhaled and is reported as the FEV1 to FVC ratio. Healthy persons generally can exhale at least 75% to 80% of their VC in 1 second and almost all of it in 3 seconds. Thus, the FEV1 normally is 80% of the FVC.

In obstructive lung disorders, such as asthma, the FEV1/FVC ratio decreased.

Pulse oximetry is a noninvasive means of assessing the degree of hypoxemia during an acute exacerbation. The oximeter measures oxygen saturation in arterial blood (Sao2) (normal $\geq 97\%$) [4] and pulse.

Peak expiratory flow rate (PEFR), obtained through the patient forcefully breathing out into a peak flow meter can be used to monitor control of asthma.

Management:

Desired Outcomes:

A. Chronic Asthma

The goal of treatment should be to obtain and maintain complete control using the least amount of medications and minimizing adverse effects.

B. Acute Asthma

Acute or worsening asthma can be life-threatening The goals of therapy are to correct significant hypoxemia, and reverse airflow obstruction rapidly.

Nonpharmacologic therapy:

Patient education is very important. Some components of asthma education involve asthma trigger avoidance, proper administration of inhaled medications, and asthma self-management. The most common cause of death from asthma is inadequate assessment of severity by the patient or physician and inadequate therapy. Thus, the key to prevention of death from asthma is education.

Avoidance of known allergenic triggers can improve symptoms and reduce medication use. Major triggers that may worsen asthma control include pollen, air pollution, cold air, exercise, strong odors, emotions, tobacco smoke, certain medications (e.g., β-blockers)

Exercise is one of the most common precipitants of asthma symptoms (exercise-induced asthma). Pretreatment with a SABA (5) minutes prior to exercise is the treatment of choice and will protect against bronchospasm for 2 to 3 hours. Regular treatment with an inhaled corticosteroid (ICS) also prevents bronchospasm associated with exercise.

A yearly influenza vaccine is recommended for patients 6 months and older with asthma to decrease the risk of complications from influenza.

Patients with aspirin-sensitive asthma are usually adults and often present with the triad of rhinitis, nasal polyps, and asthma. In these patients, acute asthma may occur within minutes of receiving aspirin or NSAIDs.

These patients are counseled against using NSAIDs. Although acetaminophen is generally safe, doses larger than 1 g may cause acute asthmatic reactions in some patients

Pharmacologic Therapy:

There are two types of asthma medications: quick-relief medications and long-term control medications.

Quick-relief medications include SABAs, anticholinergics, and short bursts of systemic corticosteroids.

Long-term control medications include ICS, inhaled long-acting β2-agonists (LABAs), oral theophylline, oral leukotriene receptor antagonists (LTRAs), mast

cells stabilizers and omalizumab. In patients with severe asthma, systemic corticosteroids may be used as a long-term control medication.

Drug Delivery Devices

Direct airway administration of asthma medications through inhalation is the most efficient route and minimizes systemic adverse effects.

Inhaled asthma medications are available in metered-dose inhalers (MDIs), dry powder inhalers (DPIs) (easier to use than MDI), and nebulized solutions.

Poor inhaler technique results in increased oropharyngeal deposition of the drug, leading to decreased efficacy and increased adverse effects.

Because MDIs are challenging to use correctly, use of spacer device is recommended with MDIs to decrease the need for coordination of actuation with inhalation, decrease oropharyngeal deposition, and increase pulmonary drug delivery.

Medications

1. Inhaled Short-Acting β2-Agonists:

Inhaled SABAs are the most effective agents for reversing acute airway obstruction caused by bronchoconstriction and are the drugs of choice for treating acute asthma and symptoms of chronic asthma as well as preventing exercise-induced bronchospasm. Inhaled SABAs have an onset of action of less than 5 minutes and a duration of action of 4 to 6 hours. salbutamol, the most commonly used inhaled SABA, is available as an MDI and solution for nebulization. During an asthma exacerbation, the usual SABA doses are doubled and the regimen changes from as needed to scheduled use.

Scheduled chronic daily dosing of SABAs is not recommended for two reasons. First, the need to use an inhaled SABA is one key indicator of uncontrolled asthma. Therefore, patients are educated to record SABA use. Second, scheduled SABA use decreases the duration of bronchodilation provided by the SABA.

2. Inhaled Long-Acting β2-Agonists:

LABAs are indicated for chronic treatment of asthma as add-on therapy for patients not controlled on low to medium doses of ICS.

Salmeterol and formoterol are LABAs that provide up to 12 hours of bronchodilation after a single dose.

Formoterol has an onset of action similar to that of salbutamol, but it is not currently approved for the treatment of acute bronchospasm.

3. Corticosteroids

Corticosteroids are the most potent anti-inflammatory agents available for the treatment of asthma and are available in inhaled, oral, and injectable dosage forms.

***A. Inhaled Corticosteroids*:**

ICS are the preferred therapy for all forms of persistent asthma in all age groups. Although some beneficial effect is seen within 12 hours of administration of an ICS, 2 weeks of therapy is necessary to see significant clinical effects. The primary advantage of using ICS compared with systemic corticosteroids is the targeted drug delivery to the lungs.

Local adverse effects of ICS include oral candidiasis, cough, and dysphonia. The incidence of local adverse effects can be reduced by using a spacer device and by having the patient rinse the mouth with water and expectorate after using the ICS.

B. Systemic Corticosteroids:

prednisolone, and methylprednisolone are systemic corticosteroids used in asthma treatment. These medications are the cornerstone of treatment for acute asthma not responding to an inhaled SABA. Because of serious potential adverse effects, systemic corticosteroids are avoided as long-term controller medication for asthma, if possible. Systemic corticosteroids are only used in patients who have failed other therapies.

4. Anticholinergics:

Two anticholinergic medications are available: ipratropium bromide and tiotropium bromide.

Inhaled ipratropium bromide is only indicated as adjunctive therapy in severe acute asthma not completely responsive to β2-agonists alone.

Tiotropium bromide is a long-acting inhaled anticholinergic available in a DPI. There is increasing evidence supporting its use as a long-term controller medication in patients with uncontrolled asthma already taking an ICS.

5. Leukotriene Receptor Antagonists (LTRAs) (Leukotriene Modifiers):

Although these agents offer the convenience of oral administration, they are significantly less effective than low ICS doses. They are not used to treat acute exacerbations and must be taken on a regular basis, even during symptom-free periods.

The available LTRAs are (zileuton, montelukast and zafirlukast). Montelukast is generally well tolerated with minimal need for monitoring and few drug interactions. Zileuton and zafirlukast are less commonly used because of the risk of hepatotoxicity. Zileuton use requires liver function monitoring prior to use, monthly for 3 months, every 3 months for the first year of use, and periodically thereafter. Zileuton and zafirlukast are metabolized through the CYP 2C9 hepatic pathway and have significant drug interactions. All three agents have reports of neuropsychiatric events, such as sleep disorders, aggressive behavior, and suicidal thoughts.

6. Methylxanthines:

Theophylline causes bronchodilation. Its use is limited because of lower efficacy as a long-term controller medication compared with ICS, a narrow therapeutic index with potentially life-threatening toxicity, and multiple clinically important drug interactions.

Methylxanthines are ineffective by aerosol and must be taken systemically (orally or IV). Sustained-release theophylline is the preferred oral preparation, whereas aminophylline is the preferred parenteral product due to increased solubility.

7. Mast Cell Stabilizers:

Cromolyn sodium (Mast Cell Stabilizer) (available as an inhalation powder and as a nebulizer solution) is indicated for prophylaxis of mild persistent asthma in children and adults.

8. Immunomodulators

Omalizumab is a recombinant humanized monoclonal anti-IgE antibody that inhibits binding of IgE to receptors on mast cells and basophils, resulting in inhibition of inflammatory mediator release. Omalizumab is indicated for treatment of patients with moderate to severe persistent asthma whose asthma is not controlled by ICS. Omalizumab significantly decreases ICS use, reduces the number and length of exacerbations, and increases asthma-related quality of life. Omalizumab is given as a subcutaneous injection every 2 to 4 weeks.

Stepwise approach for managing asthma in adults

The main principle of asthma pharmacologic step therapy is to add therapy in steps until control is achieved (step up) and decrease therapy in reverse steps (step down) to established the lowest effective dose necessary to maintain control.

Step 1: Occasional use of inhaled short-acting β2-agonist bronchodilators:

For patients with mild intermittent asthma, it is usually sufficient to prescribe an inhaled SABA, such as salbutamol or terbutaline, to be used as required.

Step 2: Introduction of regular preventer therapy:

For patients who are not controlled on a SABA alone, regular anti-inflammatory therapy (**preferably ICS**, such as beclometasone dipropionate (BDP), budesonide (BUD), or fluticasone) should be started.

Step 3: Add-on therapy:

If a patient remains poorly controlled, despite regular use of ICS; A further increase in the dose of ICS may benefit some patients but, in general, add-on therapy should be considered in adults taking 800 μg/day BDP (or equivalent).

LABAs, represent the first choice of add-on therapy. Fixed combination inhalers of ICS and LABAs have been developed; these are more convenient and increase compliance.

Step 4: Poor control on moderate dose of inhaled steroid and add-on therapy: Addition of a fourth drug:

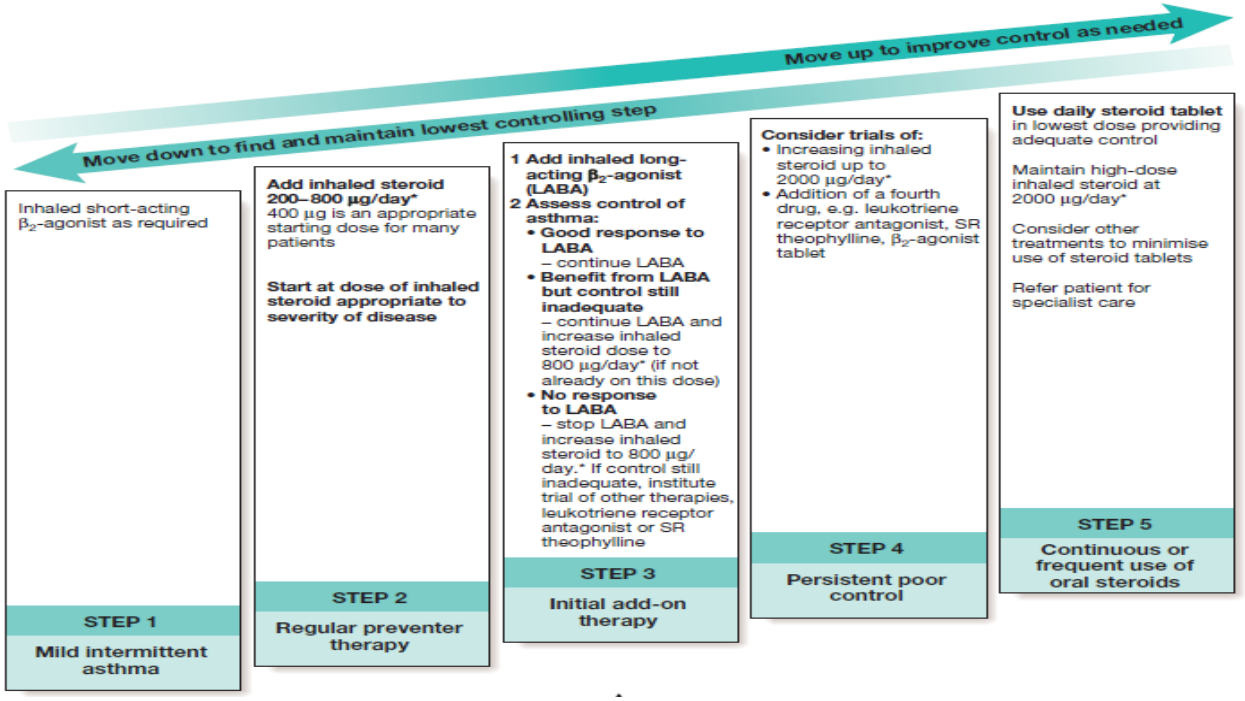
In adults, the dose of ICS may be increased to 2000 μg BDP/BUD (or equivalent) daily. Oral therapy with leukotriene receptor antagonists, theophylline or a slow-release β2-agonist may be considered.

Step 5: Continuous or frequent use of oral steroids:

At this stage, prednisolone therapy (usually administered as a single daily dose in the morning) should be prescribed in the lowest amount necessary to control symptoms.

Step-down therapy

Once asthma control is established, the dose of inhaled (or oral) corticosteroid should be titrated to the lowest dose at which effective control of asthma is maintained.



Treatment of Acute Asthma

Treatment includes the following measures:

1-Oxygen.

2-High doses of inhaled bronchodilators. Short-acting β2-agonists are the agent of choice. In hospital, they are most conveniently given via a nebulizer driven by oxygen. Ipratropium bromide provides further bronchodilator therapy and should be added to salbutamol in acute severe or life-threatening attacks.

3-Systemic corticosteroids. These reduce the inflammatory response and hasten the resolution of an exacerbation. They should be administered to all patients with an acute severe attack. They can usually be administered orally as prednisolone, but I.V hydrocortisone may be used in patients who are vomiting or unable to swallow.

Special Populations

Pregnancy

Asthma increases risk for Perinatal mortality, Preeclampsia, Preterm birth and Low birth weight infant.

Because uncontrolled asthma is a greater risk to the fetus than asthma medication use, it is safer for pregnant women to have asthma treated with medications than to experience worsening asthma. Consequently, asthma exacerbations should be managed aggressively with pharmacotherapy. The stepwise approach to asthma therapy in pregnancy is similar to that for the general population.

Salbutamol is the drug of choice for the treatment of asthma symptoms and exacerbations in pregnancy.

Budesonide has the most safety data in humans and is the preferred ICS; it is the only ICS classified as pregnancy category B. However, there are no data indicating that other ICS contribute to increased risk to the mother or fetus.

Thank You