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MANAGEMENT OF ASTHMA

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ABSTRACT

Asthma is a chronic inflammatory disorder of the airways, in which many cells play a role, in particular mast cells, oesinophills and t-lymphocytes. This inflammation causes recurrent episodes of wheezing, breathing, chest tightness and cough particularly at night or in morning. Asthma cannot be cured but it can be controlled. Better chances of asthma controlling asthma if it is diagnosed early and it treatment is begun right way. With proper treatment of asthma can have fewer and less sever attack. Without treatment of it will have more frequent and more severe asthma attacks and can even die. Better asthma control will prevent chronic and trouble ness of breath. the goal of asthma treatment is to control the disease by following the asthma action plan ,taking asthma medicines as prescribed, learning what things make your asthma worse and taking steps to avoid exposure to them, tracing your level of asthma control, and responding quick-relief medicines.

key words: asthma, chronic inflammatory, oesinophills.

INTRODUCTION

Asthma is a chronic inflammatory disorder of the airways, in which many cells play a role, in particular mast cells, eosinophills and t-lymphocytes. This inflammation causes recurrent episodes of wheezing, breathing, chest tightness and cough particularly at night or in morning (Roger walker 4th edition). Asthma is derived from the Greek word "Panos," meaning panting. By the 1800's, aided by the invention of the stethoscope, physicians began to recognize asthma as a specific disease. As early as 1892, the famous Canadian-America physician, Sir William Osler, suggested that inflammation played an important role in asthma.

Bronchial dilators first appeared in the 1930's and were improved in the 1950's. Shortly thereafter, corticosteroid drugs that treated inflammation appeared and have become the mainstay of therapy used today. Asthma is a common disease in any of the population throughout the world. In United Kingdom, it is a common disease affecting 20% of children aged 8-13 and 7% of adults. According to WHO incidents of asthma are rising by 50% every decade. In India there are an estimated 15-20 million cases of asthma in which children are the major sufferers. In India, bronchial asthma was ranked as the top killer disease in rural areas.

It affects 14 million to 15 million persons in the United States. An estimated 4.8 million children have asthma, which makes it the common chronic disease of childhood. With the increased understanding of the role inflammation plays in asthma and the addition of new pharmacological agents, the management of this disease has improved. Asthma is a cannot be cured, but it can be controlled with the asthma management. The first step in the management of asthma environmental control. There are two types groups of medications are used, first one is anti-inflammatories and bronchodilators. Anti-inflammatories are reducing the number of inflammatory cells in the airways and prevent blood vessels from leaking fluid into the airway tissues. And it also used to preventive measure to lessen the risk of acute asthma attacks. Asthma is treated with two types : first one is long – term control and quick relief medicines, long-term control medicines are used to reduce airway inflammation and preventive asthma symptoms. quick-relief medicines relieve asthma symptoms that may flare-up (Margret chandi *et al.*, 2009).

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CAUSES OF ASTHMA

Asthma should be considered in patients with a history of recurrent wheezing, cough (particularly if the cough is worse at night) recurrent shortness of breath or chest tightness.

PATHOPHYSIOLOGY

Airway inflammation is the primary problem in asthma. An initial event in asthma appears to be the release of inflammatory mediators (e.g., histamine, tryptase, leukotrines and prostaglandins) triggered by exposure to allergens, irritants, cold air or exercise. The mediators are released from bronchial mast cells, alveolar macrophages, T lymphocytes and epithelial cells. Some mediators directly cause acute bronchoconstriction, termed the "early-phase asthmatic response". The inflammatory mediators also direct the activation of eosinophills and neutrophills, and their migration to the airways, where they cause injury. This so-called "late-phase asthmatic response" results in epithelial damage, airway edema, mucus hypersecretion and hyperresponsiveness of bronchial smooth muscle. Varying airflow obstruction leads to recurrent episodes of wheezing, breathlessness, chest tightness and cough (NAEPP 1997).

PHARMACOTHERAPY

The pharmacological management of asthma depends upon the frequency and severity of asthma.

1. Reliever drugs

These are bronchodilators, give immediate relief from symptoms and are effective for 4-6 hours. They have no role in managing the inflammation.

2. Preventive drugs

These drugs prevent acute attack of bronchospasm and reduce their frequency by controlling the underlying inflammation. They begin to act within 2-3 hours and have prolonged duration of action.

Quick-Relief Medications

Short-Acting Beta$_2$Agonists

Short-acting inhaled beta$_2$agonists are the agents of choice for relieving bronchospasm and preventing exercise-induced bronchospasm. Selective beta$_2$agonists, including Albuterol, Bitolterol (Tornalate), Metaproterenol (Alupent), pirbuterol (Maxair) and Terbutaline (Brethaire) are preferred to nonselective beta agonists, such as epinephrine, ephedrine and isoproterenol (Isuprel), because the selective agents have fewer cardiovascular side effects and a longer duration of action. Inhaled beta$_2$agonists have a rapid onset of action (i.e., less than five minutes). Peak bronchodilation occurs within 30 to 60 minutes of administration, and the duration of action is three to eight hours.

Several studies have suggested that chronic daily use of short-acting beta$_2$ agonists may lead to worsening asthma control and decreased pulmonary function, particularly in moderate to severe asthma. Other studies have failed to demonstrate worsening asthma control but have shown no significant benefit from the regular daily use of beta$_2$ agonists. In light of current information, regularly scheduled daily use of short-acting beta$_2$ agonists is not generally recommended. The frequent use of quick relief medication (e.g., more than one canister per month) indicates poor control and the need for increased dosages of long-term control medications.

Systemic Corticosteroids

Short term systemic corticosteroid therapy is useful for gaining initial control of asthma and for treating moderate to severe asthma exacerbations**.** The intravenous administration of systemic corticosteroids offers is not impaired. The recommended outpatient "burst" therapy for adults is Prednisolone or methylprednisolone, prednisone in a dosage of 40 to 60 mg per day taken as one or two daily doses; for children, 1 to 2 mg per kg day to maximum dosage of 60 mg per day. Therapy is continued for three to ten days or until symptoms resolve and the patients PEF improves to 80% of his or her personal best. The oral steroid dosage does not have to be tapered after short-course "burst" therapy if the patient is receiving inhaled steroid maintenance therapy.

Anticholinergics

Ipratropium (Atrovent) is a quaternary atropine derivative that inhibits vagal-mediated bronchoconstriction. Although this drug has not been proved to be effective for long-term asthma management, it may be useful as an adjunct to inhaled beta2 agonists in patients who have severe asthma exacerbations or who cannot tolerate beta$_2$ agonists. Ipratropium has few side effects, but inadvertent eye contact can cause mydriasis.

Long-Term Control Medications

Corticosteroids

Block late-phase reaction to allergen, reduce airway hyper responsiveness, and inhibit inflammatory cell migration and activation. They are the most potent and effective anti inflammatory medication currently available. ICSs (Inhaled Corticosteroids) are used in the long term control of asthma. Short courses of oral systemic corticosteroids are often used to gain prompt control of the disease when initiating long-term therapy; long-term oral systemic corticosteroid is used for severe persistent asthma.

The dosages of inhaled corticosteroids depend on the severity of disease. Most patients can be maintained on two daily doses of the currently available preparations. Common side effects include cough, dysponia, throat irritation and oropharyngeal candidiasis. The likelihood of local side effects, especially candidiasis, can be reduced if patients use a spacer, rinse their mouth after each use and use the inhaled steroids less frequently (twice daily rather than four times daily). Higher may be associated with systemic adverse effects including adrenal suppression, osteoporosis and growth delay in children

Cromolyn sodium and Nedocromil: (Mast Cell Inhibitors)

Stabilize mast cells and interfere with chloride channel function. They are used as alternative, but not preferred, medication for the treatment of mild persistent asthma. They can also be used as preventive treatment prior to exercise or unavoidable exposure to known allergens. These agents are also used to treat mild to moderate anti-inflammatory effect. Both drugs inhibit the early-and late-phase asthmatic response to allergens and exercise. Nedocarmil appears to be more effective than Cromolyn in inhibiting bronchospasm induced by exercise, cold air and provocative testing. (Novembre G, 1994). Because of their excellent safety profiles, Cromolyn and Nedocromil are good initial long-term control medications in children and pregnant women with mild persistent asthma.

Cromolyn is available in a metered-dose inhaler (MDI), in capsules for oral inhalation and in a nebulizer solution. The usual dosages for adults are two to four puffs or one ampule of nebulizer solution three to four times daily.

Nedocromil is available only in an MDI. For adults, the dosage is two to four puffs two to four times daily for children, one to two puffs two to four daily. Four weeks of continued therapy may be required before the optimal effects of these drugs are achieved. With both agents, a single dose can be taken 15 to 30 minutes before exercise to prevent exercise-induced bronchospasm for one to two hours. Cromolyn and Nedocromil are both well tolerated although side effects such as cough, throat irritation and unpleasant taste have been reported (Lenfant C, 1995).

Salmetrol and Extended-Release Albuterol

Salmetrol (Serevent) is a long-acting beta2 agonist. Its mechanism of action and side effect profile are similar to those of other beta^{2}agonists (Laesson ML, 2001). Unlike the short-acting agents, Salmetrol is not intended for use as a quick-relief agent. It should not be used as a single agent for long-term control but instead should be used in combination with inhaled corticosteroids or other anti-inflammatory agents. Salmetrol is useful in the management of nocturnal and exercise-induced asthma. The drug is administered in an MDI in a dosage of two puffs every 12 hours. The inhalation powder formulation, Salmetrol xinafoate (Serevent Diskus), is administered in a dosage of one puff every 12 hours. Several controlled studies (Emmerton *et al*., 2003) have found that adding salmetrol to inhaled Beclomethasone dipropionate produces greater improvement in asthma symptoms and less use of rescue medications than doubling the dosage of inhaled beclomethasone.

Albuterol (Proventil Repetabs, Volmax) is available as an oral extended-release tablet for the long-term control of asthma. Like Salmetrol, this long-acting beta2 agonist is not intended to be used as a rescue medication. It is an alternative to sustained-release Theophylline or inhaled Salmetrol, especially in patients who have nocturnal asthma despite treatment with high-dose anti-inflammatory agents. Albuterol is available in 4 and 8 mg tablets. Doses are taken every 12 hours.

Theophylline

Theophylline, once the mainstay of asthma treatment, is now considered a second or third line of drug because of its adverse effect profile and potential interactions with many drugs. Furthermore, serum Theophylline levels have to be monitored during treatment. In addition to its well-known bronchodilator effects, Theophylline also has anti-inflammatory activity (Davies *et al.*, 1997).

Currently, Theophylline therapy is generally reversed for use in patients who exhibit nocturnal asthma symptoms that are not controlled with high-dose anti-inflammatory medications. These patients may benefit from the administration of a sustained-action Theophylline preparation in the evening, with the drug titrated to a serum concentration ranging from 5 to 15 µg per mL.

INHALED IPRATROPIUM BROMIDE

Ipratropium bromide is not an effective rescue medication in asthma because of its slow onset of bronchodilation effect (30-60 minutes) compared with β-2 agonists. Its role in long term asthma management has not been established, but it is useful for patients with chronic obstructive pulmonary disease. There may be an additive effect with short acting β-2 agonist during an asthma attack.

Patient response to treatment should be evaluated at least every 3 to 6 months to determine whether therapy needs adjustment. Worsening af asthma control requires a "step-up" in the treatment regimen i.e., an increase in medication dose or the addition of another medication. On the other hand, patients who have good asthma control for a period of 3 to 6 months "step down" therapy, i.e., reduce the dose or discontinue the medication.

New Agents

Zafirlukast and Zileuton

The leukotrines are potent inflammatory mediators in asthma and contribute to increased mucus production, bronchoconstriction and eosinophil infiltration. These compounds are produced via the lipoxygenase pathway by mast cells, eosinophills and alveolar macrophages. Zafirlukast (Accolate) and Zileuton (Zyflo) are two new drugs that antagonize the action of leukotrines at their receptor (Zafirlukast) or inhibit the lipoxygenase pathway (Zileuton). Both drugs are approved for the management of chronic asthma in adults and in children older than 12 years (Davies *et al*., 1997).

Zafirlukast blocks the cysteinyl leukotrines (LTD_4 and LTE_4) $CysLT_1$ receptor. This drug decreases bronchoconstriction, vascular permeability and mucus production; it has also been found to improve asthma symptoms and reduce the use of beta agonists. Zafirlukast is generally well tolerated, but headache, diarrhea, nausea and infections may occur.

Zileuton selectively and reversibility inhibits the 5- lipoxygenase pathway, preventing the formation of cysteinyl leukotrines. Therapy with this agent has improved patient symptom scores and pulmonary function tests, reduced beta-agonist and inhaled corticosteroid use, and reduced asthma exacerbations requiring corticosteroid therapy. In addition, Zileuton therapy may improve quality of life in patients with asthma (Davies *et al*., 1997).

Although Zileuton is generally well tolerated, it has the potential to elevate liver transaminase levels. Consequently, liver function should be tested monthly for the first three months of Zileuton therapy. The tests should then be repeated every two or three months for the first year of treatment. Zileuton therapy is contraindicated in patients with active liver disease. Other reported side effects include dyspepsia, headache, infections and asthma exacerbations.

Clinical experienced and studies are needed to establish their both zafirlukast and Zileuton have numerous drug interactions. Furthermore, these drugs have only been studied in patients with mild to moderate asthma. The 1997 NAEPP report suggests that these agents may be an alternative long term medication in patients older than 12 years with mild persistent asthma (step 2 therapy), but that further role in step therapy.

Asthma management:

- Prevention
- Specific Immunotherapy
- Pharmacotherapy

Prevention method:

It consists of avoidance of allergens and provoking factors.

Specific Immunotherapy:

Specific Immunotherapy (SIT) involves the administration of gradually increasing doses of allergen responsible for the patient's illness in order to induce tolerance to it, thereby reducing symptoms resulting from exposure to the allergen. It works by the principle

- An initial rise in allergen-specific IgE followed by a fall with ongoing therapy.
- Marked rises in allergen-specific IgG, especially in IgG_1 and IgG_4 subclasses.
- Decreased numbers of tissue mast cells.
- Decreased histamine reliability from basophils.
- Modification of T-cell response to the specific allergen.

There is a shift from proliferation of T lymphocytes (T helper 2 cells-TH_2), which releases from the cytokines, interleukin-4 (which favors IgE antibody production) and interleukin-5 (which induces eosinophil proliferation) to TH_1 cells.
Thus it appears that SIT results in a fundamental 'switch' from a mechanism that favors the allergic response (TH_2 induced) to one that inhibits it (TH_1 induced).

PHARMACOTHERAPY

The 1997 NAEPP report recommends a "step care" approach to asthma therapy the report discusses 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 increase treatment in steps if control is not obtained. A second and more aggressive approach is to initiate therapy at a step higher than the patient's current compare the two approaches. The NAEPP report recommends the second approach because some evidence suggests the initial aggressive treatment may yield greater clinical benefit (Lenfant C, 1995) because asthma is a highly variable disease, the physician needs to individualize treatment strategies. If initial therapy does not provide good control within one month, the treatment plan and the diagnosis should be reevaluated.

Regular follow-up visits (at one-to six-month intervals) are necessary to ensure that good control is maintained and to evaluate the need for a "step up" or "step down" in therapy. The patient should be carefully questioned about symptoms (cough, breathlessness, nocturnal symptoms, limitation in any activity) and how often quick-relief medication is used. Daily home peak flow monitoring is advised for the patient with moderate or severe persistent asthma and whenever exacerbations occur. Peak flow measurements at office visits can be useful. Spirometry should be done every one to two years to assess the maintenance of airway function.

Once asthma is well controlled, a step down in therapy is appropriate. Generally, the last medication added to the regimen is first medication withdrawn. The dosage of inhaled corticosteroids may be decreased by 25 percent every two to three months to the lowest possible dosage needed to maintain control.

Adequate asthma control may not be achieved for various reasons. The physician needs to be aware of the factors that can affect a patient's ability to control asthma symptoms. If significant exacerbations continue to occur despite efforts to control symptoms, the patient may need to be referred to an asthma specialist. Children younger than five years who have moderate or severe persistent asthma also may require referral to an asthma specialist.

At each follow-up visit, the patient should receive patient education on such subjects as adhering to medication regimens, using an inhaler and PEF meter, and controlling exposures to asthma triggers. Teaching patients self-management strategies (e.g., how to treat exacerbations, when to increase the frequency of peak flow monitoring, when to contact the physician) is vital to achieving good asthma control compliance and satisfaction (Lenfant C, 1995).

THE GOALS OF ASTHMA MANAGEMENT

- Control symptoms so as to maintain normal activity levels, including exercise.
- Maintain pulmonary function as close to normal levels as possible.
- Establish plans for the prevention and management of exacerbations.
- Avoid adverse effects from asthma medications.
- Educate patients to develop a partnership in asthma management.
- Establish plans for chronic management and regular follow-up care.
- Prevent development of irreversible airway obstruction and reduce asthma mortality by strict adherence to the above goals.

Reasons for Failure to Achieve Asthma Control

- ✓ Problems with patient adherence to treatment plan
- ✓ Problems with patient technique in using medications
- ✓ Coexisting conditions (e.g., sinusitis, allergens or irritant exposure, gastroesophageal reflux)
- ✓ Psychosocial or family barriers
- ✓ Needs for temporary increase in anti-inflammatory medication (e.g., short course of a corticosteroid)

Patient Counseling

Counseling is both an art and science because of its underlying principles and art because of the blend of the counselor's personality, technique and skill. Counseling is about helping people and as people and treatment different, there can be no universal or predetermined methods of counseling. It helps the patient to take the medication in a manner that is most likely to achieve the desired therapeutic response.

Appropriate advice, and counseling by the pharmacist will make the patient understand better about their medication which have become potent and toxic with the advancement of science this will in turn increase patient compliance, which can otherwise result in inappropriate or inadequate use of drugs,

The objective of the counseling is to provide directions, instructions, advices about the drug as per prescription and imply a positive behavior in which the patient is motivated to adheres to the prescribed treatment. Moreover, as per the new code of ethics it become the responsibility of the pharmacist to counsel the patient before dispensing of drugs in many countries.

Patient compliance

Patient compliance or adherence may be defined as the extent to which a patient takes or uses medication in accordance with the medical or health advice given.

Patients on short term medication tend to show greater compliance than those at long term therapy. In a Swedish study in late 1970's showed that patients with hypertension showed 100% compliance at the beginning, where as 94% at the end of 1st year& 34% at the end of 3rd year.

Factors effecting patient compliance

- Nature of the treatment.
- Nature of the medication.
- Characteristics of the patient.
- The type of the illness.
- The behavior of the doctor.

Pharmacist's or the counselor, lack of knowledge or information regarding medicines and health related mater constitute the leading problem in patient compliance. This is the reason why patient education is taken as a major challenge by the pharmacist engaged in patient counseling. Through patient education, the pharmacist aims at "right drug to the right patient at the right time, in the right dose through the right route, and in a right manner".

COMPLIANCE ASSESSMENT (pill count)

Compliance assessment contains a formula to calculate compliance by pill count method.

$$\text{Compliance} = \frac{\text{Total no of tablets taken} \times 100}{\text{Total no of tablets to be taken}}$$

Self assessment form contains a grading scale of compliance with this form patients will grade their compliance according to their perception,

- Almost followed prescribed regimen.
- Sometimes follow prescribed regimen.
- Compliant half of the time.
- Compliant most of the time.
- Compliant all the time.

It also contains factors which effect patient compliance.

- Forget fullness
- confusion
- Apathy
- health beliefs
- Dissatisfaction
- cost of medication
- others

Role of pharmacists and patient

The pharmacist's role is to verify that patients have sufficient understanding, knowledge and skill to follow their pharmacotherapeutic regimens and monitoring plans. Pharmacists should also seek ways to motivate patients to learn about their treatment and to be active partners in their care. Patient's role is to adhere to their dosage regimens, monitor for drug effects,

and report their experiences to pharmacists or other members of their health care teams. Optimally, the patient role should include seeking information and presenting concern that may make adherence difficult. Depending on the health system's policies and procedures, its use of protocols or clinical care plans, and its credential in of providers, pharmacists may also have disease management roles and responsibilities for specified categories of patients. This expands pharmacists and the content of education and counseling sessions.

Potential triggers	Control measures
House dust mite	Cover pillows, mattresses and box springs with zippered cases. Wash all bedding in hot water (54.4^{o}C) (130^{o}F)every10 to 14 days. Use micro filter vacuum bags. Reduce humidity levels with air conditioner. Use air filtering devices, especially and family room. Remove bedroom and family room carpeting (small, washable area rugs are an alternative)
Cockroach allergen	Cockroach extermination, preferably by professional exterminators.
Animal allergens Cat saliva and dander Dog allergens Rodent urine	Remove animal from the home, if possible (cat allergens remain in the home for up to six months after the animal is removed). When removal is not possible, confines the animal to carpet-free areas outside the bedroom and uses a high –efficiency particulate air filter.
Pollen allergens Trees Grasses Weeds	Remain indoors as much as possible during times of increased pollen levels. Use home and auto air conditioners (with closed vents) during allergy season.
Mold allergens Outdoor or "field" Fungi Indoor or "storage" Fungi	For outdoor mold, stay indoors and keep windows closed. For indoor mold, use dehumidifier in basement and air conditioners, especially in bedroom and family room. Maintain good ventilation in bathroom and kitchen.
Nonallergic airborne irritants Tobacco smoke Smoke from wood-burning stoves, fire places and other sources, fumes, strong odors	Avoid the irritants.

Fig 1. Pathophysiology of Asthma

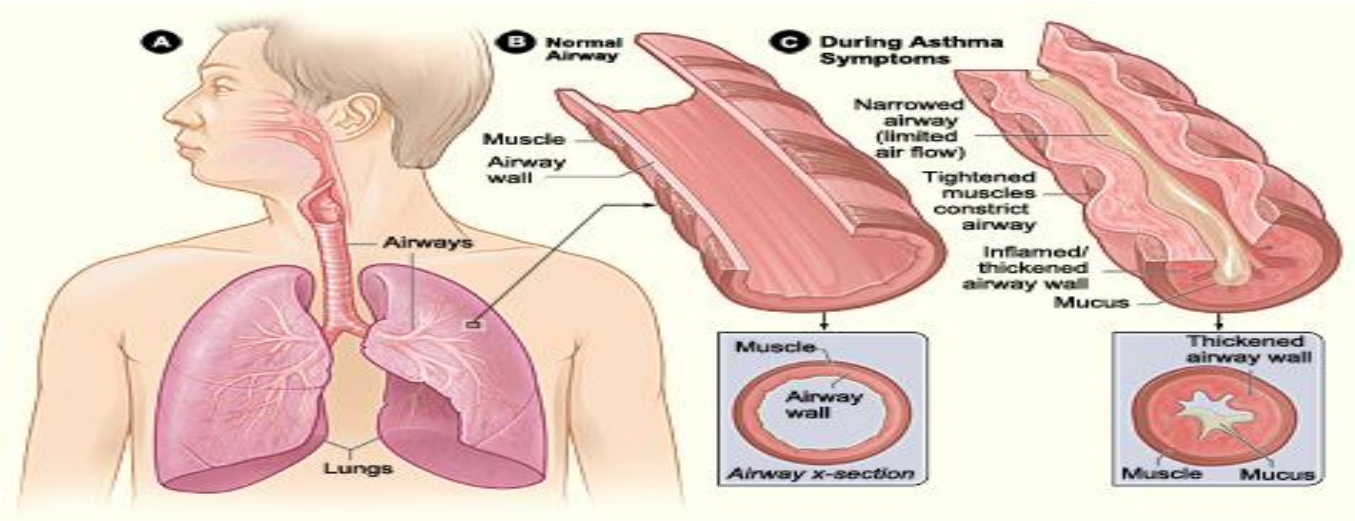

Table 1. National Asthma Education and Prevention program: Classification of Asthma Severity

Classification	Symptoms	Night Symptoms	Lung Function
Step 1 : mild intermittent asthma	Symptoms occurring twice a week or less. No symptoms and normal PEF between exacerbations. Brief exacerbations (lasting a few hours to days) with variable intensity	Symptoms occurring not more than twice a month	FEV_1/FVC is 80% or more of predicted PEF variability of less than 20%
Step 2 : mild persistent asthma	Symptoms occurring more than twice a week Exacerbations may affect activity	Symptoms occurring more than twice a week in a month	FEV_1/FVC is 80 % or more of predicted PEF variability of 20 to 30 %
Step 3 : moderate persistent asthma	Daily symptoms Daily use of inhaled short-acting beta agonist Exacerbations affect activity Exacerbations occur more than twice a week and may last for days	Symptoms occurring more than once a week	FEV_1/FVC is greater than 60% but less than 80% of predicted PEF variability of greater than 30%
Step 4 : severe persistent asthma	Continual symptoms limited physical activity Frequent exacerbations	Frequent symptoms	FEV_1/FVC is 60% or less of predicted. PEF variability of greater than 30%
PEF=peak expiratory flow; FEV_1=forced expiratory volume in one second; FVC=forced vital capacity; FEV_1/FVC%=FEV_1 as percentage of FVC.			

Table 2. Reliever drugs

Common Used Relievers	Examples
Short acting $beta_2$ agonists	Salbutamol, Albuterol, Bitolterol, Metaproterenol, Pirtuberol, Terbutaline.
Anticholinergics	Ipratropium bromide
Systemic corticosteroids	Prednisolone

Table 3. Preventive drugs

Commonly used Preventive drugs	Examples
Corticosteroids	Beclomethasone, Budesonide, Prednisolone
Mast Cell Stabiliser	Cromolyn Sodium
Long acting $beta_2$agonist	Salmetrol, Albuterol, Fomrterol, Bambuterol

CONCLUSION

It conclude that, asthma is a disease of the airways of the lungs which is characterized by increased sensitivity of the airways to a variety of triggers. So patient counseling aided better patient understanding of their illness and the role of medications in it' s treatment, improved medication adherence, knowledge and attitude regarding the disease and improved Quality of life for the patients. Moreover, a good professional report has been build between Pharmacist and patients.

The counseling service provided by clinical pharmacist was found to be useful and beneficial to the patients of the hospital where the study was carried out finally. It is believed that pharmacist and other health care professionals would appreciate the role of pharmacist in counseling and educating the patients and an attempt to extent their services to include patient counseling as one of their service.

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