Special Article

Investigation and Treatment of Asthma

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Asthma is one of the most common chronic respiratory diseases presenting with a variety of symptoms from cough, chest tightness, wheeze, difficulty breathing and in many cases persistent dyspnea. The individual has been effected usually spends a significant amount of time and financial resources in order to control the symptoms. Even though asthma has been known for more than several decades, the medications for the condition are relatively limited. This article has reviewed currently available guidelines, classifications, investigations for the diagnosis and treatment recommendations of asthma for both the general practitioners and the specialists who mainly taking care of patients with this chronic airway condition.

Keywords : *Asthma, Treatment, Investigation, Guideline*

J Med Assoc Thai 2005; 88(Suppl 4): S363-8
Full text. e-Journal: *http://www.medassocthai.org/journal*

Asthma is a chronic inflammatory disease of the airway causing an episodic variable airflow obstruction which in many cases lead to long-term bronchial hyperresponsiveness and airway remodeling[1]. The individual suffering from asthma seeks medical attention with a wide range of symptoms from intermittent cough, chest tightness, difficulty breathing to persistent dyspnea. Because asthma is one of the most common chronic respiratory diseases[2, 3], it has an effect on many patients physically by limiting daily activity, missing work or school, psychologically from living with fear of having an asthma exacerbation. It effects not only the individuals direct medical expense but also at the national level indirectly by poor productivity from uncontrolled patients. The present article has reviewed currently available investigations, treatments and practical management guideline for practitioners who have been taking care of patients with asthma.

Diagnosis of asthma

In many cases asthma is a clinical diagnosis of recurrent wheezing, coughing and chest tightness which usually occurs from an external trigger such as infection of the upper respiratory tracts, allergens, exercise, irritants, strong odor and emotional stresses. The history of intermittent obstruction of the airway presenting as cough, wheeze, difficulty breathing, limitation of exertion and night time awaking are the initial symptoms that usually bring asthmatic patients to the physician. However, there is a group of patients who have milder, intermittent symptoms of wheezing and difficulty breathing only during or after the upper respiratory tract infection. These symptoms should prompt the health care giver to further investigate into the disease. Lung function testing is helpful at least to have a baseline and confirm evidence of airway obstruction.

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Classification

Current asthma treatment guidelines from several organizations have based the classification on the severity of the disease[4, 5]. For example, the National Institution of Health and World Health Organization have published an updated report on Global Initiative for Asthma (GINA)[6] classified asthma into intermittent, mild persistent, moderate persistent and severe persistent depending on the frequency and severity of the symptoms (Table 1). It should be reiterated that severity among the individual patients can change over time. Moreover, patients in all severity may suffer from exacerbation which could be mild, moderate or severe in intensity.

Currently the treatment recommendation depends on the severity of the disease; however, there is

Table 1. Classification of asthma modified from 2004 updated GINA guideline

	Day time symptoms	Night time symptoms	FEV1
Intermittent	< 1 time/week	≤ 2 times/month	≥ 80 %
Mild Persistent	> 1 time/week but < 1 time/day	> 2 times/month	≥ 80 %
Moderate Persistent	Daily	> 1 time/week	60–80 %
Severe Persistent	Continuous	Frequent	< 60 %

evidence led to believe that the guideline may have not been followed due to the complexity of the recommendation. There are reports that goals of asthma treatment which aim to virtually eliminate all symptoms, has not been achieved even though most of the severity can be controlled if the medications have been used by the patients[7]. Thus, a future revised guideline might change the clinical outcome based treatment recommendation in which the amount of the medication used reflects the severity of the disease and total symptoms control is the primary outcome[8].

Investigation

Pulmonary function measurement can be helpful in making the diagnosis of asthma especially in the individual presenting with a nonspecific symptom such as chronic cough. Furthermore, the level of airflow limitation can be monitored during the treatment by the lung function test. To assess the pulmonary function there are two common methods used in the clinical practice. Peak expiratory flow meters measure peak expiratory flow rate (PEF) which reflects the diameter of the large airway. Although PEF is effort and measuring technique dependent, the device is small, easy to use and cheap. Because patients can use it at home to monitor their lung function, peak flow meter plays an important role in the ambulatory care of asthma[9]. Spirometry on the other hand can more accurately measure forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC) and forced expiratory flow at 25-75% (FEF_{25-75}) which are sensitive in monitoring the disease activity. The device can be used to evaluate the reversibility of the airflow obstruction after several inhalations of bronchodilator. In cases suspecting the hyperresponsive airway but found a normal initial lung function, spirometry can be helpful for an airway challenge, specifically methacholine, histamine, exercise or allergen challenge tests[10-12].

Even though pulmonary function test is extremely helpful and has been used worldwide to assist the physicians to make the diagnosis and monitoring the response to the treatment, it does have a limitation in the assessment of airway inflammation. Especially if the individual has been using a daily long acting bronchodilator may have normal lung function but whether the airway continue to have an active inflammation is difficult to evaluate without an invasive procedure such as bronchoscopy for bronchoaveolar lavarge and biopsy. Different proteins, cytokines and cells in the peripheral blood have been studied in the attempt to find the surrogate markers of airway inflammation but most of them are neither specific nor practical[1, 13]. Sputum eosinophil has been the first marker known to have a significant correlation with asthma symptoms at the same time the measurement is simple. It is not only correlated with the disease activity but can also be used to predict the control of asthma [14]. The sputum collection and eosinophils staining technique does not require a special tool other than what is already available in most standard hospital laboratories.

Exhaled nitric oxide is a measurement of the amount of nitric oxide gas in the exhaled air. It has been proved to be well correlated to the inflammation of the airway and can be used to both monitor and adjust the medication use in patients with asthma [15]. The procedure, however, is technically difficult to do in a general internal medicine office. In the future when the smaller and cheaper version of nitric oxide measuring machine becomes available it may change the way we monitor the symptoms of asthmatic patients[16].

Treatment

Nonpharmacological treatment includes awareness of risk factors triggering asthma, detecting the early sign of exacerbation, understanding the medication and if necessary seeking medical help are the important part of management[6]. Well informed patients do well in both when the symptoms are under good control and when an exacerbation occurs[9]. Written personal asthma management plan should always be made available to the individual patient even though it may not always be helpful in every case [17, 18]. Some of the risk factors that can be controlled to avoid unnecessary exposure are listed below (Table 2).

Pharmacological treatment of asthma has been divided to medicine use to immediately relieve the

bronchocontriction and thus called "reliever". The main medication in this class is the beta-2 agonist bronchodilator which has a quick onset of action. Patients usually feel the brochodilating effect within minutes after the use of the inhaler. Currently there are several bronchodilators that not only have a quick onset of action but also have a long duration of effects. Some of these medications have been used concomitantly with the controller medication, inhaled corticosteroid, to increase anti-inflammatory effects of the corticosteroid.

Controller medicine includes cromones, inhaled corticosteroids (ICS), leukotriene modifiers, theophylline, long acting beta 2 agonists (LABA) and systemic corticosteroids (Table 3, 4). Because of excellent safety profile cromolyn sodium and nedocromil are commonly used in mild persistent disease in children and occasionally in patients who become pregnant. Because these medicines are hydrophilic and have a short half life, they have to be used two to four times a day in order to be effective.

Table 2. Aggravating factors commonly worsening asthma symptoms

Respiratory tract infection i.e. rhinovirus
Irritant i.e. aerosol chemicals
Tobacco smoke
Allergens
· Dust mites
· Cockroach allergens
· Animals with fur
· Pollens
· Molds
Drugs
Emotional stress

Table 3. Inhaled corticosteroid in asthma

Inhaled Steroid	Usual recommended dose/day
Beclomethasone	200-1000 microgram
Budesonide	200-1000
Fluticasone	100-500
Mometasone	200-800
Flunisolide	500-2000
Triamcinolone	400-2000
Ciclesonide	160 -320

Table 4. Other controller medicine

Other controller	Usual recommended dose / day
Cromolyn	1-2 puffs bid to qid
Nedocromil	1-2 puffs bid to qid
Montelukast	10 mg daily
Theophylline	200 mg daily - bid
Zafirlukast	20 mg bid
Formoterol	1-2 puffs bid
Salmeterol	1-2 puffs bid

The inhaled steroid is considered to be the main controller medication proved to be safe, well tolerated, effective in lowering frequency of asthma exacerbations, emergency room visits and hospital admissions from severe exacerbation (Table 3). It has been recommended for use in a stepwise approach starting with a low dose of inhaled corticosteroid in mild persistent asthma and stepped up to the higher dose or add another controller if symptoms persist. Arecent report, however, has been contradicted to the previous guideline and showed that in longstanding mild persistent adult asthma, using an inhaled corticosteroid intermittently may have the same benefit of daily use [19].

Theophylline is a xanthiene oxidase inhibitor which has been used in asthma for several decades. Previously the bronchodilator effects were the main reason that it was used in a high dose. Recently, the anti-inflammatory effects were found by the possible effect on the histone deacetylation [20]. Thus, a lower dose of theophylline has been recommended for asthma. Leukotriene receptor inhibitor or enzyme modifier is a new class of asthma controlling medicine inhibiting either at the enzyme lipoxeginase or leukotriene receptor inhibition. Although the effects seem to be a little less compared to ICS, leukotriene modifiers have gained popularity among pediatricians in the last few years due to the better compliance from the once or twice daily oral form.

Long acting beta 2 agonist (LABA) initially was used as an added on controller medicine in those asthma symptoms which are not well controlled by ICS alone[21]. It later found that LABA, with an uncertain mechanism, does increase the efficacy of ICS when used in a separate inhaler and it seems to further enhance these effects if they are combined in the same device[22-24].

Humanized monoclonal anti-IgE antibody, omalizumab, is an antibody which specifically binds to the Fc portion of immunoglobulin E leading to the reduction of the total IgE and IgE receptors. This novel antibody has been approved in the US for use in patients suffering from severe asthma. Anti-IgE antibody has been evaluated in clinical studies and shown to be effective in severe steroid dependent asthma[25], reduced rate of exacerbation and emergency room visit[26]. It has been looked at in other conditions such as mild asthma, allergic rhinitis[27], anaphylaxis[28], atopic der-

matitis[29] and concomitant uses with immunotherapy the result of which are promising[30]. Because of the price and the route of administration, the use of current anti-IgE, however, remain to be seen.

Phosphodiesterase (PDE) inhibitor is a newer class of medicine that is under investigation in asthmatic patients. It may help to control asthma by inhibiting PDE enzyme, decrease oxidative stress and airway inflammation. It has a potential in asthma management because of the better compliance due to the oral form of this medicine[31].

Immunotherapy has been recommended in asthmatic patients who also have allergy as a major cause of exacerbation [32]. It is conventionally given in subcutaneous form either slowly increasing the dose to the maintenance level or by rush methods in which the level can be reached in days. The maintenance should be continued for three to five years in order to modify the immunological response to the given allergen. Sublingual immunotherapy has been recommended mainly in Europe due to the convenience. To have the same effect of the conventional subcutaneous immunotherapy, the amount of the allergens used in sublingual immunotherapy has to be increased more than five to ten times. The effects in asthma are marginal at the current data[33].

In conclusion, asthma is a chronic respiratory disease causing several different symptoms. Asthmatic patients may have been affected in both health and financial issues. The early diagnosis, investigation and proper treatment may improve the outcome of treatment. Both nonpharmacological and pharmacological treatment have an important role in the care of the chronic condition. A few newer classes of medicine are under investigation which may be available in the near future.

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การตรวจวินิจฉัยและรักษาโรคหืด

ฮิโรชิ จันทาภากุล

โรคหืด เป็นโรคทางเดินหายใจที่มีอาการเรื้อรังและพบบ่อย ผู้ป่วยจะมาพบแพทย์ด้วยอาการที่แตกต่างกันไป ตั้งแต่ ไอ แน่นหน้าอก มีเสียงวี๊ดในปอด หรือหายใจลำบากตลอดเวลา ผู้ป่วยมักจะมีความสูญเสียทั้งเวลาและการเงินเพื่อรักษาโรค ถึงแม้ว่าโรคหืดจะเป็นที่รู้จักมานาน แต่ยาที่ใช้รักษายังจำกัด บทความนี้ได้รวบรวมแนวทางในการรักษา การแบ่งความรุนแรงของโรค การวินิจฉัยและยาที่ใช้รักษาโรคหืด ซึ่งน่าจะเป็นประโยชน์ต่อทั้งแพทย์เวชปฏิบัติทั่วไป และแพทย์ผู้เชี่ยวชาญที่ดูแลผู้ป่วยโรคหืดอยู่เป็นประจำ