Basic Pharmacotherapy for Asthma

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In order to appropriately utilize pharmacologic agents in the treatment of asthma, it is essential to recognize that asthma is a chronic condition that is characterized by intermittent exacerbations. Prevention or minimalization of exacerbations is a primary goal in the management of asthma. This involves avoidance of known triggers of asthma; in allergic patients, minimization of cat or dog allergen exposure would be an example. In patients with mild, intermittent asthma and very rare exacerbations, occasional use of a β-agonist metered dose inhaler (MDI) will generally suffice. On the other hand, patients with moderate asthma, which is characterized by long-term exercise intolerance and frequent symptoms, will require regular asthma medications.

Another primary goal in the management of asthma is anticipatory or early treatment of exacerbations in order to prevent the development of severe airway obstruction. An example would be prescribing a short course of oral steroids to an asthmatic patient who has developed a viral upper respiratory infection that is beginning to cause a significant exacerbation.

Immunotherapy is not, strictly speaking, a pharmacologic agent. Rather, its mechanism of action in the treatment of allergic rhinitis and extrinsic asthma is probably immunologic. In certain cases of extrinsic asthma, immunotherapy should be considered; a complete review of immunotherapy for extrinsic asthma is beyond the scope of this article, but can be found elsewhere.

Patient education is also a major aspect of asthma management. An informed patient who understands the chronicity of asthma, how to avoid asthma triggers, how to use medications, and when to call the physician, is a key element in the optimal management of asthma.

Scientific Rationale for Asthma Pharmacotherapy

The pharmacotherapy of asthma should be directed at the underlying pathophysiology and should be tailored to the disease severity. It is recognized that airway inflammation and hyperresponsiveness are important aspects of asthma, and thus, the use of antiinflammatory drugs has increased significantly. In addition, there is development of new therapeutic agents directed at reducing airway inflammation and hyperreactivity. Bronchospasm is a well-recognized aspect of asthma, and thus, bronchodilators are an important part of the therapeutic armamentarium of asthma treatment.

Asthma management requires clinical experience and judgment; it cannot be reduced to a simple formula. The protocols outlined by the National Heart, Lung and Blood Expert Panel are, however, useful as a first approximation for treatment of asthma based on severity.

Pharmacotherapy for Mild Asthma

Patients can be classified as having mild asthma if they have short, infrequent (<2 times per week) episodes of asthma with normal exercise tolerance between attacks. Those patients generally fare well with β-agonist MDI administration as required and prior to stimuli, such as exercise or allergen exposure. Cromolyn MDI alone or in combination with β-agonists is also useful prior to known asthma triggers, such as allergens or exercise. In general, MDI administration of a β-agonist is preferable to oral administration in that efficacy is similar but adverse effects are significantly less. There is a report that associates regular use of β-agonists with inadequate asthma control. However, there are multiple other reports of improvement with regularly administered β-agonists. Whenever a MDI is prescribed for a patient, the patient should be instructed in its use, and inhaler technique should be assessed. Studies have indicated that up to one half of patients use the MDI improperly. In patients to whom inhaler technique cannot be taught, a spacer will often allow medication administration by MDI.

Pharmacotherapy for Moderate Asthma

In patients who have moderate asthma, the above protocol will give inadequate relief because medications are required daily. Those patients have symptoms more than twice a week, have inadequate exercise tolerance at all times and have occasional emergency visits for uncontrolled asthma. There is a growing opinion that steroids administered by MDI should be the primary treatment for asthma that requires prolonged medication. The usual doses are approximately 400 to 800 μg beclomethasone per day, but there is evidence to support higher doses in adults, even up to 2,600 μg per day. There are very rare reports of systemic adverse effects; local adverse effects include oral thrush, dysphonia, and cough.

Another antiinflammatory agent, cromolyn, might be used instead of, or in addition to, aerosolized corticosteroids. Cromolyn has the advantage of having virtually no adverse effects. However, its effectiveness is not as reliable as that of inhaled corticosteroids. A 4 to 6 week trial may be required to ascertain whether improvement will occur in an individual patient. Inhaled β-agonists, up to 2 puffs 4 times a day, would also be prescribed with the antiinflammatory agent(s).
Nedocromil sodium is a drug that is not currently approved by the FDA but is undergoing clinical trials. It inhibits mediator release in vitro, inhibits early and late phase allergen responses, and reduces airway hyperreactivity. Its place in the asthma therapeutic armamentarium remains to be defined.

Some physicians might use sustained release theophylline in addition to or in lieu of a β-agonist. However, increased reports of severe adverse effects from theophylline have tempered theophylline use considerably. In patients in whom theophylline is prescribed, monitoring of serum concentration is an important part of management. While optimal bronchodilator effect occurs with 10 to 20 µg/ml, aiming for levels between 5 and 15 µg/ml will likely reduce incidence of adverse effects. Signs and symptoms of theophylline toxicity include nausea, vomiting, tachyarrhythmia, diuresis, inattention especially in children, and seizures.

The place of anticholinergic medications in asthma is not clear. While some asthmatics respond acutely to anticholinergics, some do not, and the peak onset of bronchodilation is much slower in onset, up to 90 min.

PHARMACOTHERAPY FOR ASTHMA EXACERBATIONS

In spite of the above interventions, asthma may still not be controlled. In the mild to moderate asthmatic, this most commonly occurs in the face of a viral upper respiratory infection. A burst of oral corticosteroids (30 to 60 µg daily) for 5 to 7 days will often be effective. Some patients will require a tapering alternate day schedule over 1 to 3 weeks, but many will tolerate cessation of oral corticosteroid without any tapering.

If the control achieved with oral corticosteroids is short-lived (less than 2 to 3 weeks), the patient will likely require prolonged alternate day prednisone. The exact dose can be determined by using a tapering schedule that does not reduce the dose more than once a week.

The major adverse effects of short-term, high dose steroids include increased appetite, fluid retention, and mood alteration. Long-term corticosteroid therapy is associated with risk of osteoporosis, hypertension, cataracts, diabetes, proximal myopathy, and pituitary-adrenal axis suppression. The lowest possible dose of alternate day corticosteroids should therefore be used to minimize adverse effects. As with any medication use, risks and benefits must be carefully evaluated.

CONCLUSIONS

Pharmacotherapy is a very important aspect of the management of asthma. Other important aspects are avoidance of known triggers of asthma, such as allergens, and patient education. Pharmacotherapy of asthma should be directed at the underlying pathophysiologic condition and should be tailored to the disease severity. In particular, airway inflammation and hyperresponsiveness of asthma are best treated with antiinflammatory drugs. Examples of such drugs include inhaled corticosteroids, oral corticosteroids, and cromolyn. Bronchospasm is another well-recognized aspect of asthma. Examples of medications that primarily act as bronchodilators are β-agonists and theophylline. While treatment of asthmatic patients cannot be reduced to a simple algorithm, a general approach adapted from the NHLBI Expert Panel Report is outlined for the management of mild and moderate asthma.

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