

ABSTRACT

The common airway diseases comprise asthma and chronic obstructive pulmonary disease (COPD). Pharmacologic treatment with inhaled corticosteroids is the mainstay of management in most patients with asthma. Inhaled bronchodilators are the foundation of pharmacotherapy for COPD. This is because of their capacity to alleviate symptoms, decrease exacerbations of disease, and improve quality of life. In either condition, combination therapy with inhaled corticosteroids and long-acting beta2-agonists may be beneficial for more severe disease. Oral theophylline also has a significant role in obstructive airway disease. This article summarises the key pharmacologic agents that are useful in obstructive airway disease.

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DRUG THERAPY IN AIRWAY DISEASE

Asthma is defined as a condition characterised by recurrent or chronic wheeze and/or cough, with recognisable variable airway obstruction due to bronchial hyper-reactivity secondary to airway inflammation. While asthma exacerbations may be episodic, the airway inflammation is chronically present. Pharmacologic treatment with inhaled corticosteroids is the mainstay of management in most patients with asthma.

COPD on the other hand is a slowly progressive condition, mostly occurring in smokers, with patients diagnosed usually in their 60s, with little variability in symptoms and limited response to bronchodilators or corticosteroids. Inhaled short-acting bronchodilators are recommended as first-line therapy in COPD to relieve symptoms and improve exercise capacity. This unit will discuss the pharmacology of drugs commonly used in obstructive airway disease.

INHALED SHORT-ACTING BRONCHODILATORS

The drugs most commonly used for the treatment of pulmonary diseases are bronchodilators, and they are the mainstay for prompt reversal of bronchospasm. Short-acting inhaled beta2-agonists remain the treatment of choice for acute exacerbations of asthma, and for preventing exercise-induced bronchospasm¹. In patients with mild intermittent asthma, short-acting inhaled beta2-agonists are recommended as quick-relief medication for treating symptoms as needed.

For relief of mild bronchoconstriction, beta2-agonists are typically taken as two puffs from a metered-dose inhaler every 4-6 hours as needed, but patients should be instructed to take higher doses at more frequent intervals for persistent or severe symptoms while starting additional treatment (e.g. with oral or inhaled corticosteroid) or seeking a higher level of care. The frequency of use of rapid-acting inhalers is an indication of the degree of control of asthma, as use of more than one canister of a beta2-agonist per month has been associated with increased risk for death or near death from asthma². Occasionally, inhaled salbutamol may be associated with tremor, palpitations or tachycardia, which is much less than would occur with oral beta2-agonists.

Inhaled bronchodilators are the foundation of pharmacotherapy for COPD because of their capacity to alleviate symptoms, decrease exacerbations of disease, and improve quality of life. These drugs also improve airflow and hyperinflation^{3,4}, thereby decreasing the work of breathing and improving exercise tolerance. For patients with mild airflow limitation and intermittent symptoms, a single short-acting inhaled bronchodilator relieves symptoms and improves airflow.

Salbutamol and ipratropium are equally effective with regard to bronchodilation and symptoms scores and can be used interchangeably for mild disease as the first step in a series of measures for treating patients with COPD. Combination bronchodilator therapy (an anti-cholinergic agent plus a beta2-agonist) may be considered for patients in whom a single inhaled bronchodilator has failed to provide adequate relief.

INHALED LONG-ACTING BRONCHODILATORS

Inhaled bronchodilators can be grouped according to their duration of action. Long-acting beta2-receptor agonists such as formoterol fumarate and salmeterol xinafoate have an effect for 8-12 hours, and the long-acting anti-cholinergic agent tiotropium bromide has a duration of effect of more than 24 hours. Long-acting beta2-agonists are currently recommended as adjuncts to anti-inflammatory medications in asthma, when a low to medium dose of inhaled corticosteroids alone fails to achieve adequate control of asthma¹.

For COPD, they may be added to the treatment regimen when symptoms are not controlled with short-acting inhaled bronchodilators alone. Regular treatment with one or both classes of the inhaled long-acting bronchodilators should also be considered for patients with moderate to severe COPD with frequent exacerbations⁵. Tiotropium is the only long-acting anti-cholinergic currently available, for treatment of COPD. It

has been shown to be effective in reducing acute exacerbations, reducing symptoms and improving health-related quality of life compared to placebo and to ipratropium bromide.

INHALED CORTICOSTEROIDS

Inhaled corticosteroids (ICS) are recommended as the initial and primary therapy in all patients with persistent asthma. Several randomised, prospective studies have demonstrated that ICS improve symptoms, improve lung function, decrease need for short-acting bronchodilators and improve airway responsiveness to methacholine in patients with all levels of asthma severity⁶⁻¹⁰. They will not cure asthma, and if they are stopped for any reason, the symptoms of asthma with deterioration will usually recur. Observational data also suggest that ICS diminish hospitalisations and mortality from asthma¹¹⁻¹³. The actual dose prescribed can be titrated depending on the severity of asthma and degree of control. The side effects of ICS include oropharyngeal candidiasis, dysphonia and cough. Inhaled corticosteroids are best used at low to moderate doses.

For COPD, current evidence supports limiting the use of ICS to patients with moderate to severe disease and who have frequent exacerbations⁵. Inhaled corticosteroids have only a modest effect on lung function in COPD, and individual long-term studies have shown that they do not affect the rate of FEV1 decline in COPD of all severity grades.

COMBINATION THERAPY

The addition of inhaled long-acting beta2-agonists (LABA) to ICS therapy can improve asthma symptoms and reduce exacerbations¹⁴. The addition of LABA may also have an ICS-sparing effect and permit a reduction in ICS maintenance dose. Adult asthmatics with symptoms not controlled with 400-800 mcg of inhaled corticosteroids per day should be given a LABA. The addition of the LABA results in better asthma control, and reduction in severe exacerbations when compared with doubling the dose of inhaled corticosteroids.

In COPD, combination therapy with ICS + LABA should be considered for patients in whom both its components are indicated⁵. The combination formulation will be more convenient and will aid compliance in patients for whom both an ICS and LABA are indicated.

THEOPHYLLINE

Oral theophylline, a non-specific phosphodiesterase inhibitor, has been used for more than 50 years for the treatment of obstructive airway diseases. In addition to its bronchodilator function, it has effects on the respiratory muscles, mucociliary clearance, ventilator drive, and has immunomodulatory properties.

Regular use of theophylline decreases the frequency and severity of asthmatic symptoms in patients with chronic asthma.

It reduces the 'as needed' use of inhaled beta2-adrenergic agonists and of short courses of corticosteroids, and prevents exercise-induced bronchoconstriction. Sustained-release theophylline's main use is as adjunctive therapy, and it is particularly effective for controlling nocturnal symptoms of asthma. It may be useful as an add-on drug in patients who do not achieve good control on ICS alone.

For COPD patients, it may be useful when symptom control is still not achieved with existing inhaled bronchodilator therapy. Since theophylline may be toxic, frequent monitoring for supratherapeutic levels, adverse drug reactions, and drug interactions is important.

LEUKOTRIENE MODIFIERS

Leukotriene modifiers such as montelukast are safe and well tolerated in asthma. They have a small and variable bronchodilator effect, reducing asthma symptoms, exacerbations, and airway inflammation and improving lung function. It can either be used as an alternative to low dose ICS in patients with mild persistent asthma, or as an add-on drug when low dose ICS or when combination of ICS +LABA has not achieved the desired effect.

ORAL STEROIDS

A rescue course of oral steroids is indicated for acute exacerbations of asthma. They prevent the progression of asthma exacerbation, reduce the need for emergency room treatment, reduce the need for hospitalisation and prevent early relapse after acute treatment. Long-term use of low doses of oral steroids is associated with increased risk of adverse effects and should not be used in primary care.

A short course of oral steroids should also be considered in COPD patients who have an exacerbation with a significant increase in the breathlessness that interferes with daily activities. Long-term oral steroids are not recommended in stable COPD.

OTHER THERAPIES

Antibiotics, antihistamines, mucolytics and anti-tussives have no special role in asthma therapy. In stable COPD, there is also currently no evidence to support the benefit of routine use of maintenance antibiotic therapy, mucolytics, anti-oxidants, vasodilators or leukotriene modifiers.

CONCLUSIONS

Inhaled corticosteroids are the most effective anti-inflammatory medications available for the treatment of persistent asthma. They are taken on a daily basis. Short-acting inhaled beta2-agonists are the relievers of choice for an acute asthma episode. They work rapidly, and are taken only

when required. The frequency of use of rapid-acting inhalers is an indication of the degree of control of asthma. The addition of a LABA to ICS results in better asthma control, and reduction in severe exacerbations when compared with doubling the dose of ICS, for asthma that is not controlled on low to medium dose of ICS. Inhaled bronchodilators are the foundation of pharmacotherapy for COPD. Inhaled long-acting bronchodilators may be added to the treatment regimen for COPD when symptoms are not controlled with short-acting inhaled bronchodilators alone.

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LEARNING POINTS

- **Pharmacologic treatment with inhaled corticosteroids is the mainstay of management in most patients with asthma.**
 - **Avoid excessive use of short-acting beta2-agonists in asthma due to association with risk of asthma death.**
 - **The addition of LABA to ICS results in better asthma control, and reduction in severe exacerbations when compared with doubling the dose of ICS, for asthma that is not controlled on low to medium dose of ICS.**
 - **Inhaled bronchodilators are the foundation of pharmacotherapy for COPD.**
 - **Inhaled long-acting bronchodilators may be added to the treatment regimen of COPD when symptoms are not controlled with short-acting inhaled bronchodilators alone.**
 - **For COPD, current evidence supports limiting the use of ICS to patients with moderate to severe disease and who have frequent exacerbations.**
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