Oral vs Inhaled Asthma Therapy
Pros, Cons and Combinations

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Summary

A number of oral and inhaled drugs are available for the long term management of patients with persistent asthma, yet the disease continues to be associated with significant morbidity and mortality. Over the past years, inhaled glucocorticoids have become established as a cornerstone of maintenance therapy because of their demonstrated clinical efficacy, ability to reduce bronchial inflammation and good tolerability. Other inhaled drugs (e.g. sodium cromoglycate, nedocromil, long-acting β₂ agonists) also play a role in the long term treatment of patients with asthma. However, many patients (especially children and the elderly) find inhalers difficult to use, and poor inhalation technique can affect the amount of drug reaching the lungs and response to therapy. Oral drug administration is simple, but, until recently, oral asthma therapy has primarily consisted of sustained-release theophylline and glucocorticoids. Theophylline has a narrow therapeutic index, necessitating regular monitoring of serum drug concentrations, and long term oral glucocorticoid therapy is associated with potentially serious adverse events including osteoporosis with bone fracture. The recent development of orally administered leukotriene receptor antagonists (e.g. zafirlukast) and 5-lipoxygenase inhibitors (e.g. zileuton) offers novel mechanisms of action and potential solutions to compliance issues associated with regular administration of inhaled asthma therapy. These drugs have demonstrated efficacy as maintenance therapy in patients with asthma and, importantly, lack the adverse effects associated with long term systemic glucocorticoid therapy. Further clinical trials and the increasing use of these new therapies will help to establish the precise role of orally administered leukotriene receptor antagonists and 5-lipoxygenase inhibitors in the long term management of patients with asthma.

Asthma is an inflammatory disorder of the airways and one of the most common chronic diseases in industrialised countries. Despite the availability of a myriad of oral and inhaled asthma medications, the prevalence of asthma and its associated mortality continue to increase. Asthma is also associated with significant morbidity, often affecting the patient’s normal daily activities, disturbing normal sleep patterns and potentially reducing quality of life. Patients with poorly controlled asthma present a medical challenge that remains far too prevalent, and this may be partly related to suboptimal treatment strategies and poor patient compliance with drug therapy. Current treatment guidelines (which are discussed in another paper in this supplement) help to ameliorate these problems, and the development of new agents, such as orally administered leukotriene inhibitors.
receptor antagonists, may also lead to improved management of patients with asthma.

With a few exceptions, such as parenterally administered aminophylline and salbutamol (albuterol), most drugs used in the treatment of patients with asthma are administered orally or by inhalation. This article reviews the positive and negative aspects of oral and inhaled asthma medications, including issues relating to patient compliance, pharmacokinetic properties, clinical efficacy, tolerability and the use of these medications in combination.

1. Patient Compliance with Oral vs Inhaled Therapy

Although asthma cannot be cured, the severity of the disease can be reduced with long term anti-inflammatory therapy. Compliance with long term therapeutic regimens is difficult and, as indicated in another paper in this supplement,[8] is affected by a number of factors, including the frequency and ease of drug administration as well as adverse events. Obviously, patient compliance with therapy for any chronic disease such as diabetes mellitus or hypertension is important; however, compliance with asthma therapy has the added dimension that treatment frequently includes the use of inhalers, which are relatively complicated devices and which many patients (especially children and the elderly) find difficult to use.[9,10] Indeed, it has been shown that the great majority of elderly patients cannot use inhalers properly, despite adequate instruction.[11]

The most widely used aerosol delivery system is the pressurised metered-dose inhaler (pMDI), although the use of dry powder inhalers has increased in recent years.[9,12] Efficient delivery of drug to the lungs by pMDI requires correct positioning of the inhaler, a slow inspiratory flow rate, the synchronisation of canister actuation with inhalation, and holding of the breath (for about 5 to 10 seconds) at the end of inspiration.[9,12] Various errors can occur with pMDI use, such as incorrect timing of actuation, and these are summarised in table I. Poor inhalation technique can affect the amount of drug reaching the lungs and response to therapy.[13-17] For example, slow inhalation (30 L/min) of terbutaline sulfate, administered by pMDI, achieved a greater increase in forced expiratory volume in one second (FEV1) than fast inhalation (90 L/min).[15] Consequently, patients may become noncompliant with therapy because of difficulty using the inhaler or because the treatment is perceived as not being effective.[9,12]

Various spacer devices and valved holding chambers are available to improve or simplify inhalation technique with pMDIs, although they do not eliminate the need for correct inhalation technique.[9,12] Some patients, particularly adolescents, may not wish to use such a device (especially in public places).[18] Another potentially useful device is the breath-activated pressurised inhaler (Autohaler®), which avoids the need to coordinate aerosol discharge with inhalation.[12,19] Similarly, dry powder inhalers are designed to release the medication powder on inhalation, but require a relatively high inspiratory flow rate to release a full dose.[12] As a result, dry powder inhalers are probably more suitable for maintenance therapy than for rescue from severe asthma exacerbations (when patients have decreased airflow), and children aged