EDITORIAL OVERVIEW

Decision making in asthma therapy—what is important in clinical practice?

Although the prevalence of asthma is rising around the world, the disease remains poorly controlled despite the availability of highly effective anti-asthma therapies. Failure to follow asthma management guidelines, patient non-compliance with therapy, and inhaler misuse (particularly pressurised metered dose inhalers (pMDIs)), contribute to this lack of disease control. The implementation of asthma management guidelines is improving, but until these guidelines are adhered to, asthma will often remain poorly controlled. As it is unlikely that asthma therapy will improve significantly in the near future, advances in inhaled drug delivery have become an important aspect of improving asthma management. An inhaler device which improves patient compliance would represent a major step forward in asthma management. Dry powder inhalers (DPIs) preclude the need to coordinate inspiration with activation, are easy and convenient to use and are environmentally friendly.

A satellite symposium held during the 13th Annual Congress of the European Respiratory Society in Vienna Austria, from 27 to 31 September 2003, reviewed several issues surrounding the management of patients with asthma. In particular, how to measure the effects of inhaled corticosteroids (ICSs) in clinical studies; how to assess long-term asthma control in clinical practice; the importance of the inhaler device and how this has recently been improved; new data on key parameters for effective use of DPI systems and; how to achieve good compliance with inhaled asthma therapy were reviewed.

Asthma is a highly complex inflammatory disease of the airways involving many inflammatory cells and their mediators. ICSs are the gold standard anti-inflammatory therapy for asthma and have been studied in numerous different clinical trial designs such as long-term comparative studies, retrospective steroid tapering and mortality studies, combination studies and dose–response studies. The effectiveness of ICSs has also been assessed using allergen challenge models and by measuring their effect(s) on airway hyper-responsiveness and exhaled nitric oxide (NO) concentrations. Results have shown that ICSs are more effective in controlling asthma than β-agonists or leukotriene agonists. Steroid tapering induces asthma exacerbations, whilst the regular use of low doses of ICSs prevents death from asthma. ICSs show a modest dose response for lung function, symptom control and oral corticosteroid use, are effective in reducing airway hyper-responsiveness to various stimuli, and reduce exhaled NO concentrations and the number and activation state of a wide variety of inflammatory cells. Finally, using allergen challenge models even single doses of ICSs have profound inhibitory effects on the late asthmatic reaction.

Although highly effective treatments for asthma are readily available (e.g. ICSs and long-acting β₂-agonists), the prevalence and incidence of asthma continues to rise around the world and the disease remains poorly controlled. Asthma control may be improved by the use of assessment tools which monitor asthma control and detect exacerbations before the alteration of functional parameters and the occurrence of symptoms. Effective monitoring of asthma control would enable clinicians to increase corticosteroid dose or to stop corticosteroid tapering before symptoms occur. Tools to assess asthma control must be reproducible, acceptable to patients, non-invasive, and suitable for long-term use. Tools currently used include clinical parameters (e.g. symptom scores, nocturnal awakenings and rescue medication use), lung function, questionnaires, bronchial hyper-responsiveness, sputum eosinophilia and exhaled NO. Sputum
exhaled NO and sputum eosinophilia is useful for preventing exacerbations from occurring in the first instance and may help to achieve asthma control in the long-term.

Lack of asthma control may be caused by many factors such as non-implementation of asthma management guidelines and patient non-compliance with prescribed anti-asthma therapy. The Global Initiative for Asthma (GINA) guidelines defines asthma control and recommends therapeutic strategies to attain control of the disease. However, the guidelines are frequently not implemented as they do suffer from many inherent limitations. Treatment regimens should take into account patients’ ‘real-life’ conditions in order to realistically tackle the disease. Non-compliance with therapy is another major reason why asthma remains poorly controlled. The reasons for non-compliance are complex and involve drug and non-drug factors. In the non-drug category, inability to use inhaler devices correctly is a common cause of non-compliance.

pMDIs are the most frequently prescribed inhaler devices despite the fact that they are inefficient, difficult to use correctly, require extensive training and retesting, have no inhalation control system, no dose counter and are environmentally unfriendly. In fact many patients and even health care professionals cannot use them correctly, mainly due to problems coordinating inhaler activation with inspiration. An inhaler device which improves patient compliance would be a major technological advancement. Criteria that may improve patient compliance with an inhaler are: correct use of the device by most patients, accurate and consistent dose release (even at low inspiratory flow), feedback to the patient that the drug has been inhaled, ease and convenience of device use, availability of cartridge refills and overall convenience in the device. DPIs have several advantages over pMDIs. They are breath-activated, easy and convenient to use and environmentally friendly.

There is no doubt that the type of inhaler is just as important as the class of drug in the long-term management of asthma. Improvements in inhaled drug delivery will continue to be important in improving asthma management. Three key parameters for successful inhaler use should be considered when evaluating existing or future DPI devices: (1) compliance; (2) fine particle fraction (FPF) with relatively little dependence on inspiratory flow and; (3) clinical efficacy. A threshold mechanism which controls for a minimal inspiratory flow rate is desirable in order to support formation of an optimal FPF and related lung deposition. Additionally, in order to enhance patient compliance a multi-dose DPI should feature a visual or acoustic feedback of a successful inhalation. The GINA guidelines recommend DPIs or breath-activated pMDIs for children older than 6 years. They recommend that inhalers should be portable and simple to operate, should not require power, require minimal cooperation and coordination and have minimal maintenance requirements. The device itself should deliver an accurate and consistent dose throughout its lifetime. It should be easy and convenient to use, easy to teach, deliver a range of molecules, have an accurate dose counter, give patient feedback and be conveniently carried, robust, visually appealing and chlorofluorocarbon-free.

The articles that follow discuss several factors that influence asthma management. The first article (pp. S4–8) reviews the GINA guidelines as to what constitutes asthma control, assesses the current status of asthma control and discusses many reasons why asthma, despite many pharmacological and technological advancements, remains a poorly controlled disease. The article by Hansel assesses the various clinical trial designs used to assess the efficacy of ICSs in asthma. Magnan (pp. S16–21) discusses many objective and subjective tools used to measure asthma control and Richter (pp. S22–27) describes the design features of the Novolizer® (VIATRIS, Germany). Clinical data examining the suitability of the Novolizer® for use in children, and data comparing the peak inspiratory flow rate generated through the Novolizer® and the Turbuhaler® in adults with moderate-to-severe asthma or chronic obstructive pulmonary disease is also reviewed. Virchow (pp. S28–34) reviews the factors which influence clinician decisions regarding which therapy and which device to prescribe to patients. Finally, Crompton (pp. S35–40) reviews the problems associated with pMDIs and DPIs currently on the market, discusses factors likely to improve patient compliance and examines how the novel features of the Novolizer® could improve patient compliance.

The symposium concluded that inhaled therapy is likely to remain predominant in the future and that the type of inhaler is just as important as the class of drug in the long-term management of asthma in adults and children. Despite the availability of highly effective anti-asthma therapies, the disease remains poorly controlled, most likely due to non-implementation of asthma management guidelines
and non-compliance due to inhaler misuse. An inhaler device which improves patient compliance with therapy would be a major technological advancement and an important step forward in asthma management. The Novolizer® is a multidose refillable DPI with multiple feedback mechanisms, a unique trigger flow valve system, low intrinsic resistance and particle size is relatively independent of inspiratory flow rate. It is a device which is tolerant of poor patient technique and has many features which may improve patient compliance.

Peter J. Barnes
Department of Thoracic Medicine, National Heart and Lung Institute, Imperial College School of Medicine, Dovehouse Street, London SW3 6LY, UK
E-mail address: p.j.barnes@ic.ac.uk