Relievers, controllers, and inhaler technique: A physician-patient challenge

Physicians and patients often have different views and perspectives of what constitutes well-controlled asthma. Although patients are routinely informed about the use of inhalers for treatment of their asthma, physicians sometimes overestimate the patient’s competence and knowledge of optimal inhaler usage. True to the publication of diverse issues that comprise and challenge the field of allergy and immunology, the allergist/immunologist and the patients we serve, this issue of the Proceedings features a spectrum of articles that addresses this challenge. We hope this issue will provide greater insight that will lead to improved management of the patient with asthma.

The unmet need attributable to the management of uncontrolled asthma is well established. Although inhaled controller therapy can be very effective, not all patients respond. One of the most common reasons for therapeutic failure is suboptimal inhaler technique. Asku et al. set out to determine the rate of incorrect inhaler technique among patients with pulmonary diseases and the efficacy of delivering physician-provided inhaler training to patients. The study involved 108 patients, and 158 different inhalation techniques were assessed. Despite finding a high prevalence (41%) of inappropriate inhaler use, the authors reported an 80% success rate when physicians provided practical training.

Because of the high prevalence of suboptimal inhaler technique, alternate delivery systems have evolved to include multidose dry powder inhalers (MDPI). Within this issue are three articles that report the safety, efficacy, and pharmacologic characteristics of MDPI treatment. Qaqundah et al. demonstrated the comparability of albuterol MDPI and albuterol hydrofluoroalkane in children with asthma. Ratnayake et al. compared the pharmacokinetics, pharmacodynamics, and tolerability of albuterol MDPI and hydrofluoroalkane after a single inhaled dose in children with asthma. In a phase III, 12-week study, Amar et al. evaluated the safety and efficacy of beclomethasone dipropionate hydrofluoroalkane, BAI, and metered-dose inhaler (MDI) versus placebo in patients who previously used a mid-to high-dose inhaled corticosteroid (ICS) or ICS–long-acting β agonist (LABA) for persistent asthma.

In the setting of adequate inhaler technique in moderate-to-severe persistent asthma, when asthma control is not achieved on ICS alone, current guidelines recommend a step-up regimen of combination therapy with an ICS and an LABA. These two agents are thought to enhance the pharmacologic action of each other by a synergistic effect. With the goal of testing this hypothesis, Shimoda et al. compared a group of patients who used ICS monotherapy with a group treated with the ICS-LABA combination and evaluated the effect of the LABA on the anti-inflammatory action of the ICS. Although the ICS-LABA combination group experienced significantly greater improvement in lung function and airway hyperresponsiveness than the ICS monotherapy group, the two groups did not show significant differences in changes in FeNO or the percentage of sputum eosinophils, which indicated that a synergistic effect of the LABA on enhancing the anti-inflammatory action of the ICS was not clinically apparent.

An alternative to ICS controller therapy for mild persistent asthma, is a leukotriene receptor antagonist; however, it is unknown what effect this class of agents may have on airway remodeling. Tenero et al. set out to evaluate the effect of montelukast treatment on sputum markers of airway inflammation and remodeling in children with mild asthma. Measured markers included MM-9, MM-12, TIMP-1, TGFβ1, PICP, and eosinophil count. The authors report a significant reduction of PICP levels and eosinophils in sputum after treatment with montelukast, which supported the hypothesis that montelukast can modulate collagen deposition in airways and reduce eosinophilic airway inflammation.

In another study of asthma biomarkers in children, Stelmach et al. evaluated biomarkers in schoolchildren with exercise-induced symptoms. Biomarker assessment included measurement of FeNO, serum tryptase, and exhaled breath condensate, together with a spectrum of proinflammatory cytokines and eicosanoids. Their results confirmed the role of mast cells and eicosanoids in the pathogenesis of exercise-induced bronchoconstriction in children.
Allergy skin testing is a procedure that dates back to the early decades of the 20th century and remains the most useful tool for the in vivo assessment of sensitization to specific allergens. However, some patients may be worried about pain associated with skin-prick testing. In a reassuring survey study, Coop and Forster reported that the actual pain experienced from skin-prick testing was perceived to be much less than the anticipated pain. The authors indicated that patients should not fear the potential pain that results from allergy skin-prick testing.

Shifting from lower airway to upper airway disease, Klimek et al. presented the results of a real-life assessment of MP-AzeFlu by using a visual analog scale, in a large pan-European population of 2988 patients (≥12 years) with ARIA-defined moderate-severe allergic rhinitis (AR). They reported evidence that MP-AzeFlu provided effective and rapid symptom control in a real-life pan-European setting and indicated that MP-AzeFlu is the drug of choice for the treatment of moderate-severe AR.

Given the global efforts directed at reducing health care costs, Lang et al. provide a timely assessment of health care resource use and associated costs among patients with seasonal versus perennial AR. They reported that patients with perennial AR experienced more AR-related prescription drug use and higher health care costs than patients with seasonal AR, with prescription drug costs being the main cost driver.

In transitioning to urticaria, one of the most challenging and poorly understood cutaneous diseases for which the allergist/immunologist offers expertise, Magen et al. sought to identify clinical and laboratory patient attributes that may be predictive of the progression of acute spontaneous urticaria to chronic spontaneous urticaria. By studying 114 patients with acute urticaria without identifiable causes, the researchers reported that patients with acute spontaneous urticaria who progressed toward chronic spontaneous urticaria were characterized by a positive autologous serum skin test, thyroid autoimmunity, and profound basophilopenia at baseline.

Chronic urticarial and other allergic diseases can also aggravate stressors that affect psychiatric conditions. From this perspective, Heath et al. conducted a pilot study of anxiety and depression in a cohort of adult patients with primary immunodeficiencies (PID) by asking “How much do these patients experience and how much do they attribute to their PID?” The authors reported finding that many factors influenced depression and anxiety in this clinical setting and may add to the morbidity of PID. They indicated that patients with PID should be assessed for risk factors (identified in their study) for depression and anxiety, and treatment or appropriate referrals should be initiated. Because of the importance of this article and its clinically useful implications, it was chosen for this issue’s “For the Patient” section. This segment, found in the final pages of the print version of this issue and also available online, consists of a one-page article synopsis written in a readily comprehensible fashion to help patients better understand the content of the full article.

Allergy immunotherapy dates back to 1911 and the pioneering contributions of Noon and Freeman. Advancement of knowledge regarding its efficacy and safety continues to remain a special focus of the Proceedings. This issue contains two articles that help to fill this void, one that focuses on the safety of subcutaneous allergen immunotherapy and the other focuses on the safety of oral immunotherapy. With regard to the safety of subcutaneous allergen immunotherapy, certain underlying medical conditions, such as HIV infection, malignancy, and severe asthma, may be considered to impose an elevated risk for untoward outcomes, but, unfortunately, no guiding data exist. To gauge this concern, Larenas-Linnemann et al. conducted a Web-based survey among members of the American Academy of Allergy, Asthma & Immunology. The authors reported that, according to the experience of a large group of practicing allergists, very few medical conditions (e.g., severe asthma, AIDS) seemed to pose an elevated risk for untoward outcomes from subcutaneous allergen immunotherapy.

With regard to the safety of oral immunotherapy, Pajno et al. described the occurrence and characteristics of adverse events with oral immunotherapy, based on their experience conducting controlled trials in children with milk and egg allergies. The authors reported that adverse events are not rare but that ~90% of children can achieve an effective desensitization. They cautioned that the procedure remains investigational and should be performed only by trained physicians.

Finally, addressing the utility of the electronic medical record in allergy/immunology practice, Zelig et al. sought to improve physician knowledge and management of food allergies by implementing educational and electronic medical record interventions. Their report disappointingly demonstrated that neither intervention resulted in improved management of children with food allergies.

In summary, the collection of articles found within the pages of this issue provides further insight into important allergic, cutaneous, and respiratory disorders that afflict patients whom the allergist/immunologist serves. In keeping with the overall mission of the Proceedings, which is to distribute timely information regarding advancements in the knowledge and practice of allergy, asthma, and immunology to clinicians entrusted with the care of patients, it is our hope that the articles found within this issue will help foster enhanced patient management and outcomes. On behalf of the
editorial board, we hope you enjoy the diversity of literature offered in this issue of the Proceedings.

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