EDITORIAL

Montelukast and Fluticasone Therapy in Patients with Mild Persistent Asthma

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Mild persistent asthma (MPA) is widely prevalent in men and women of all racial and ethnic groups throughout the world. Asthma is an inflammatory disorder affecting the tracheobronchial tree and can be associated with atopy and allergic rhinitis. In response to a variety of environmental, occupational, and pharmacologic triggers, patients with asthma develop airway obstruction secondary to bronchial mucosal edema, smooth muscle cell contraction and spasm, and increased mucus and inflammatory mediator expression. The increased expression of inflammatory mediators such as histamine, leukotrienes, and prostaglandins is mediated by mast cells and macrophages resident within the respiratory tract.

The suppression of inflammation is an important component in the management scheme for achieving control of asthma-related symptoms. Systemic and inhalational steroids have been used to control asthmatic exacerbations in the acute and chronic settings, respectively. More recently, with the increased recognition that leukotrienes play a prominent role in potentiating the inflammatory response within the respiratory tract, leukotriene receptor antagonists (LRAs) have assumed a significant place in the management of patients with MPA. As with many other disease states, the management of asthma frequently depends on the initiation of polypharmacy to achieve optimal, durable control of such symptoms as nocturnal and daytime wheezing and dyspnea. Treatment with multiple drugs enables clinicians to beneficially intercept multiple pathways etiologic for disease onset and progression. Although inhalational steroids are widely regarded to be safe and have been shown to reduce risk for developing adverse airway remodeling and loss of airway responsiveness, concerns about their systemic effects continue to linger.

In this issue of *The Journal of Applied Research*, Bousquet and coworkers evaluate the relative efficacy of the LRA montelukast and the inhalational steroid fluticasone in controlling symptoms in patients with MPA also using a ?-agonist as needed for acute breakthrough. In a large (645 patients), long-term (48 week) randomized prospective trial, these authors demonstrate that both of these medications provided statistically significant symptom improvement. While montelukast did not achieve the endpoint for noninferiority compared to fluticasone, it is apparent that over the course of the trial, the relative superiority of fluticasone for increasing asthma-free days and decreasing the need for acute rescue medication became less significant over time. Of interest is the finding that, among patients with low frequency of ?-agonist use, there was no difference between the two groups.

The effects of chronic inflammation likely require sustained periods of therapy in order to reverse accumulated tissue damage. Had the study gone longer, perhaps the differences between treatment arms would have decreased still further and even equalized.

Consistent with this is the observation that improvement in quality of life was greater at 12 weeks in patients treated with fluticasone, but by 36 weeks there was no difference between the two treatment groups.

In a variety of important disease measures, montelukast provided as much benefit as did fluticasone and adverse event rates were similar in both treatment arms. Consistent with previous studies, in patients with MPA montelukast is efficacious, reduces eosinophilia as well as steroid therapy, and significantly reduces the need for rescue medication. Additional studies may help to better delineate: (1) how much the LRAs reduce steroid requirements in patients with more moderate and severe persistent asthma; and (2) if certain subgroups of patients with specific leukotriene receptor subtypes or mast cell characteristics benefit proportionately more from LRA therapy.

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