Clinical application of Montelukast in Korean children with persistent asthma.

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A considerable increase in the prevalence of childhood asthma over the last few decades has been demonstrated. Concerns have been expressed about the development of tolerance with continuous use of beta-agonist bronchodilators and about the potential adverse systemic effects of high-dose inhaled corticosteroids in children.

Most of long-term experience in treating children with asthma is with inhaled corticosteroids; however, these agents are most notably (1) the fact that they do not block the release of cysteinyl leukotrienes in asthma (2) their potential for adverse effects on growth and skeletal development when used in high doses in children and (3) difficulties in achieving adequate compliance with their use.

The leukotriene receptor antagonists (LTRAs) selectively block the binding of cysteinyl leukotrienes to the CysLT1 receptor, which has been identified as the receptor through which most of their actions are mediated. These actions include bronchoconstriction, mucus hypersecretion and increased vascular permeability and eosinophil migration. Consequently, the LTRAs inhibit bronchoconstriction.

In a large, placebo controlled pediatric trial, the leukotriene receptor antagonists (LTRAs) significantly reduced requirements for rescue beta-agonist bronchodilators, improved quality of life, reduced the circulating level of blood eosinophils and produced improvements in lung function. In adult studies, LTRAs reduced sputum eosinophils and attenuated early and late phase allergen induced reactions. The LTRAs also produce bronchodilator effects that are additive to those of beta-agonists and decrease requirement for use of these drugs.

Moreover, LTRAs prevent many types of provoked asthmatic responses, including allergen induced, cold air hyperventilation induced, and aspirin induced asthma. LTRAs have also demonstrated protective effects against exercise induced bronchospasm in both adults and children, and this protection was maintained during the trough period at the end of the once daily administration interval.

Several studies have demonstrated that the formation of cysteinyl leukotrienes in the airways of asthmatic patients is not suppressed by corticosteroids, so LTRAs demonstrate complementary effects when given with inhaled corticosteroids. Currently, leukotriene receptor antagonists can be used as add-on therapy to inhaled corticosteroids to allow tapering of corticosteroid dose and reduction in beta-agonist use. Recent clinical trial results suggest also be a role for these agents as first-line therapy in children with mild asthma.
As well as their additive effects with beta-agonists and inhaled corticosteroids, the LTRAs may also produce an additive effect with H1-antihistamines in inhibiting allergen induced early and late phase airway obstruction in asthmatics.

In a multicenter, clinical efficacy of montelukast (5 mg once daily) was studied in 212 asthmatic children aged 6-14 years for 8 weeks of treatment. Significant and consistent improvements over the 8-week treatment period were observed in asthma symptom scores (severity, frequency, daily activities and sleep) and beta-agonist use & need for rescue therapy were significantly reduced. Asthma-specific quality of life parameters improved with after 8 weeks of montelukast treatment.

These properties, LTRAs produce effects additive to those of inhaled corticosteroids and permit long term reductions in corticosteroid dosage, suggest that LTRAs are an attractive option for complementary therapy in patients with chronic persistent symptoms who have a suboptimal response to low-to-moderate doses of inhaled corticosteroids or who are poorly adherent to this therapy. International guidelines already include LTRAs in their recommendations for managing asthma.