Which patients with asthma could benefit from using anti-leukotriene drugs: an evidence based review

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Asthma is characterized by airway inflammation, bronchial hyperresponsiveness and airway obstruction. Many mediators and cytokines have been found involved in the pathogenesis of asthma. Leukotrienes are produced via the 5-lipoxygenase pathway of arachidonic acid metabolism. Monocytes, alveolar macrophages, and peripheral blood neutrophils preferentially generate leukotriene B4 (LTB₄), whereas eosinophils, mast cells and basophils preferentially generate the cysteinyl leukotrienes (CysLTs) (LTC₄, LTD₄ and LTE₄).¹

The CysLTs have been strongly implicated in the pathogenesis of asthma and allergic rhinitis. They are potent bronchoconstrictors and have many proinflammatory effects, such as the recruitment and activation of eosinophils, increased vascular permeability and stimulation of airway mucus secretion.²

The CysLTs bind to the leukotriene receptors CysLT1 and CysLT2. Most of the actions of the CysLTs are believed to be mediated through the CysLT1 receptor. The advent of the leukotriene modifiers including the CysLT1 receptor antagonists provided a relative new class of antiasthma drugs.³

Montelukast as add-on therapy to inhaled corticosteroids in the treatment of mild to moderate asthma: a systematic review

Many clinical trials have shown CysLT1 receptor antagonists to be effective in asthma therapy. As inhaled corticosteroids (ICS) are more effective in reducing asthma
of life, treatment satisfaction, physical capacity, asthma related mortality and total mortality. It is of importance to note that, in contrast to the previous Cochrane reviews, in this systematic review short-term trials with duration of less than 12 weeks were excluded.

Overall the findings of this systematic review indicate that montelukast/ICS was clinically more effective than ICS monotherapy. The combination montelukast/ICS was however clinically less effective than the combination salmeterol/ICS in the 12 week trials. A separate analysis of active controlled 48 week trials showed comparable proportions for patients with at least 1 exacerbation in both groups.

Conclusion  Antileukotriene drugs are now considered as an alternative to low dose of inhaled steroids in step 2 and as an alternative to long acting β₂-agonists for add-on to inhaled corticosteroids in step 3 and 4 of the GINA guidelines. The systematic review reported by S. Joos et al. from Heidelberg underscore the value of montelukast in the step 3 and 4 of the 2006 guidelines. As the contribution of different asthma mechanisms (inflammation and bronchial hyperresponsiveness) differs among different patients (or in individual patient over time) benefit of any drug in an individual patients may differ as well and individualized therapy is frequently needed.

**REFERENCES**