Review: antileukotrienes are less effective than inhaled corticosteroids in chronic asthma


QUESTION: In patients with chronic asthma, are daily antileukotrienes (ALs) as safe and effective as inhaled corticosteroids (ICSs)?

Data sources
Studies were identified by searching Medline (1966–2002), EMBASE/Excerpta Medica (1980–2002), CINAHL (1982–2002), the Cochrane Airways Group register of randomised controlled trials (RCTs), the Cochrane Controlled Trials Register (to January 2002); checking the reference lists of all relevant trials; contacting the pharmaceutical companies that manufacture ALs; and contacting colleagues and trialists in the field of paediatric asthma.

Study selection
Studies were selected if they were RCTs comparing daily oral ALs at usual licensed doses with any type of ICS in children ≥2 years of age and adults with chronic asthma. Interventions had to be administered for ≥30 days.

Data extraction
Data were extracted independently by 2 reviewers blinded to identifying information about the study on quality (randomisation, blinding, and description of withdrawals and dropouts), patient characteristics, drug type and dosage, and outcomes. The primary outcome was the rate of asthma exacerbations requiring systemic corticosteroids. Secondary outcomes were other indicators of exacerbation severity (hospital admissions), asthma control measures (change from baseline FEV1), morning peak expiratory flow, symptom score, nocturnal awakenings, quality of life, and β2 agonist use, adverse effects, and withdrawal rates.

Main results
14 trials met the inclusion criteria (8 full text, 1 in press, and 5 abstracts). 12 trials were done in adults, 1 was in adults and adolescents (≥12 y), and 1 was in children (mean age 10 y). The duration of the intervention ranged from 4–37 weeks. The ALs tested were montelukast, pranlukast, and zafirlukast. 11 trials reported the rate of exacerbation in mild persistent asthma. From pooled data of the 14 RCTs comparing ALs with ICSs as monotherapy in mild persistent asthma, ALs were less effective than ICSs in preventing asthma exacerbations requiring rescue oral steroids. However, no differences existed for more severe exacerbations requiring hospitalisation. This complemented other data that suggest minimal further benefit in adding ALs to ICSs and that question taping of ICSs.1

The meta-analysis by Ducharme and Hicks further strengthens the argument that ICSs should be used as first line treatment in mild persistent asthma. From pooled data of the 14 RCTs comparing ALs with ICSs as monotherapy in mild persistent asthma, ALs were less effective than ICSs in preventing asthma exacerbations requiring rescue oral steroids. However, no differences existed for more severe exacerbations requiring hospitalisation. This complemented other data that suggest minimal further benefit in adding ALs to ICSs and that question taping of ICSs.1

The main issue to consider when interpreting data from clinical trials directly comparing ICSs and ALs is the large interpatient variability in response to all asthma medications, including ICSs.2 Group mean data favour ICSs over ALs, but the individual response to ALs varies.3 Such heterogeneity in response cannot currently be predicted from clinical parameters. As our understanding of pharmacogenetics improves, it may allow tailoring of medication regimens to suit individual patients according to probable response. Until then, ICSs at the minimum effective dose should be recommended as first line therapy for mild persistent asthma. ALs may be considered as an alternative to ICSs in patients with mild persistent asthma if compliance with inhaled medication is in question or if ICSs are associated with unacceptable oropharyngeal side effects.


Commentary

Antileukotrienes (ALs) vs inhaled corticosteroids (ICSs) for chronic asthma at 4–37 weeks*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Weighted event rates</th>
<th>ALs</th>
<th>ICSs</th>
<th>RRI (95% CI)</th>
<th>NNH (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1 asthma exacerbation requiring systemic corticosteroids</td>
<td>8.9%</td>
<td>5.9%</td>
<td>61% (15 to 125)</td>
<td>34 (17 to 334)</td>
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</tbody>
</table>

*Abbreviations defined in glossary; RRI, NNH, and CI calculated from data in article using a random effects model.

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Abstract and commentary also appear in ACP Journal Club.