Review: regular inhaled long acting $\beta_2$ agonists are associated with better outcomes than short acting $\beta_2$ agonists in adults and children with chronic asthma


QUESTION: What is the effectiveness of regular inhaled long acting $\beta_2$ agonists compared with inhaled short acting $\beta_2$ agonists in adults and children with chronic asthma?

Data sources
Studies were identified using the Cochrane Airways Review Group register, which is derived from searching Medline, CINAHL, and EMBASE/Excerpta Medica. In addition, bibliographies of relevant studies were scanned, key respiratory care journals were hand searched, and experts were contacted.

Study selection
Randomised controlled trials of $\geq 2$ weeks duration were selected if they compared a regular inhaled long acting $\beta_2$ agonist with a regular inhaled short acting $\beta_2$ agonist of equivalent (as far as possible) bronchodilator effectiveness in adults or children with chronic asthma (ie, those with a diagnosis of $\geq 6$ mo). Studies including participants with other pulmonary diseases or using oral $\beta_2$ agonists were excluded.

Data extraction
Data were extracted in duplicate on study quality, methods, participants, interventions, and outcomes.

Main results
31 studies met the selection criteria. 24 studies used a parallel group design, and 7 used a crossover design. Long acting $\beta_2$ agonists assessed were salmeterol xinafoate (22 studies) and formoterol fumarate (9 studies). Short acting $\beta_2$ agonists assessed were salbutamol sulphate (26 studies) and terbutaline sulphate (5 studies). Treatment duration ranged from 2 to 24 weeks. Participants were $> 12$ years of age in 28 studies and $< 12$ years of age in 3 studies. Most studies (n=23) included participants with mild to moderate asthma. 25 studies permitted concomitant treatments, primarily inhaled corticosteroids or cromones.

Patients who received long acting $\beta_2$ agonists had better outcomes than those who received short acting $\beta_2$ agonists in terms of lung function, symptom scores, percentage of days and nights without symptoms, and use of rescue bronchodilators (table).

Conclusion
In adults and children with chronic asthma, regular inhaled long acting $\beta_2$ agonists are associated with better physiological and clinical outcomes than short acting $\beta_2$ agonists.

COMMENTARY
Although asthma is highly variable in presentation, regular daily treatment is often required. Tolerance to the bronchoprotective effect of both long and short acting $\beta_2$ agonists has been shown.1 Walters et al examined studies that compared the effects of regular use of inhaled long acting $\beta_2$ agonists with inhaled short acting $\beta_2$ agonists. This important clinical question has dimensions of benefits, harms, and costs. The review addressed a clear question, had a comprehensive search strategy, clear inclusion and exclusion criteria, and used the Jadad scale for rating methodological quality. 3 studies involved children $< 12$ years of age, and data from these studies were combined with studies of adults for the results reported in the tables. The review provides comparisons of some outcomes for children, but each comparison is based on only 1 study, limiting the applicability of the results for children.

Sears reports that the pharmacologically predictable effects of both short and long acting $\beta_2$ agonists are not problematic,2 except perhaps in the presence of hypoxia or comorbidity, and tolerance to these effects occurs readily. This review by Walters et al assessed, where data were available, adverse reactions, and found no statistically significant difference in total adverse effects, mortality, or individual adverse effects except for headache. These findings are important, given previous concerns about increased mortality with the use of $\beta_2$ agonists.

The authors conclude that inhaled long acting $\beta_2$ agonists are associated with better physiological and clinical outcomes than short acting $\beta_2$ agonists. However, the studies were of short duration. It would be useful to see if treatment of longer duration shows adequate benefit relative to costs and adverse effects.