Review: inhaled long acting β₂ agonists are effective and safe in stable chronic asthma


Clinical impact ratings GP/FP/Primary care ★★★★★☆☆ Internal medicine ★★★★★☆☆ Allergy ★★★★★☆☆☆☆☆☆ Respiriology

In people with stable chronic asthma, are inhaled long acting β₂ agonists [LABAs] effective and safe?

In people with stable chronic asthma, inhaled long acting β₂ agonists were effective and safe.

CONCLUSION

After a single inhalation, the bronchodilating effects of LABAs last ≥ 12 hours. However, their safety has been debated in the scientific literature for > 10 years.

The systematic review by Walters et al used a comprehensive search strategy and rigorous review methods. They concluded that LABAs improve symptoms, spirometry, and asthma exacerbations when compared with no LABAs. Subgroup analysis showed greater benefit in patients already on inhaled corticosteroids. However, pooled data in children (5 RCTs) suggested an increased risk of exacerbation with LABAs. Their regular use was associated with a bronchoprotective effect of 1.5 to 1.8 doubling doses of methacholine.

The review overlooks several important issues. Firstly, heterogeneity in airway inflammation was not considered. LABAs may not clear anti-inflammatory effects and may mask a smouldering eosinophilic inflammation, particularly when the inhaled corticosteroid dose is also reduced. Well conducted RCTs have shown that LABA monotherapy can worsen asthma. Thus, the clinical relevance of a comparison with placebo becomes doubtful. Secondly, studies have not compared full and partial agonists. Development of tolerance to the bronchoprotective effect may be more likely with a full agonist than with a partial agonist, particularly in patients who are homozygous for arginine in codon 16 of the β₂ receptor gene. Indeed, a recent analysis found that the adverse effects of salmeterol monotherapy were greater in this set of patients (presented at the 2004 National Heart Lung Blood Institute Workshop on Clinical Research in Asthma).

In summary, although this meta-analysis shows a benefit for LABAs relative to placebo, insufficient evidence exists to recommended monotherapy with LABAs. They can be considered as add on therapy for patients who are symptomatic on moderate doses of inhaled corticosteroids or even after airway eosinophilic inflammation is controlled. The role of genetic polymorphism of the β₂ receptor in predicting adverse outcomes and the role in children need further evaluation.

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