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Title **Long-acting ß2-agonists for Maintenance Therapy of Stable Chronic Obstructive Pulmonary Disease: A Systematic Review**

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Aim

To assess the efficacy and safety of salmeterol and formoterol for maintenance treatment of patients with stable, non-reversible chronic obstructive pulmonary disease (COPD), as compared to:

- Placebo (with or without the additional use of short-acting ß2-agonists)
- Anticholinergics (with or without the additional use of short-acting ß2-agonists).

Conclusions and results

A systematic review identified 58 potentially relevant studies. Of these studies, 9 described trials that satisfied the eligibility criteria (6 were of moderate quality and 3 of low quality as assessed on the Jadad scale). The trials reviewed compared salmeterol and formoterol both to placebo and to the older alternative agent, ipratropium bromide. Because of differences in trial design and reporting, meta-analysis of quantitative outcome measures was not possible. Rather, a best-evidence-synthesis approach was used. Among patients with less than 15% improvement in FEV1 (forced expiratory volume in one second) after a single dose of short- or long-acting bronchodilator, reviewers found that the long-acting ß2-agonists were superior to placebo in decreasing the use of a rescue inhaler. Although an increase in FEV1 was also observed, there was no improvement in functional outcomes such as distance traveled in a 6-minute walking test. Reviewers found little evidence regarding the effects of these agents on COPD exacerbations and on health-related quality of life. The two studies, both of moderate quality that compared the new agents with ipratropium bromide did not show salmeterol and formoterol to be more efficacious. Safety data were not reported in any of the studies reviewed.

Methods

Published and unpublished reports were identified by three methods: a) searching multiple databases and web sites; b) hand searching selected journals, documents, and bibliographies of selected papers; and c) contacting the manufacturers of salmeterol and formoterol. Regardless of publication status, studies using both parallel and cross-over designs were included as long as the duration of therapy was at least 4 weeks. The eligibility criteria for trial participants included non-asthmatic, stable COPD, an FEV1 of 75% or less than predicted, an FEV1 /FEV (forced vital capacity) ratio less than 70% predicted, and less than 15% improvement in FEV1 after a dose of a short- or long-acting ß2-agonists. Two reviewers independently made decisions about study inclusion, quality, and data extraction.

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