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Title **Long-acting ß 2-agonists for the Maintenance Treatment of Chronic Obstructive Pulmonary Disease in Patients with Reversible and Non-Reversible Airflow Obstruction: A Systematic Review of Clinical Effectiveness**

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Aim

To critically examine the clinical effectiveness of inhaled long-acting ß 2-agonists in patients with stable chronic obstructive pulmonary disease (COPD) and reversible or non-reversible airway obstruction.

Conclusions and results

Thirty-three unique trials were identified, 64% were of higher quality (Jadad ≥3).

Long-acting ß 2-agonists did not have any significant advantages over placebo in reducing mortality and upper respiratory tract infections, or in improving exercise capacity and tolerability. Compared with placebo, long-acting ß 2-agonists have a demonstrated effect in reducing COPD exacerbations and hospitalizations in patients with mild to severe COPD. Long-acting ß 2-agonists did not demonstrate a significant advantage compared with either anticholinergic agent in most functional outcome measures. Salmeterol is not as well tolerated as tiotropium. No data were available to compare the tolerability of formoterol with tiotropium.

Recommendations

Not applicable.

Methods

Published literature was identified by searching electronic databases from 1992 onward. Grey literature was obtained by searching the websites of health technology assessment and related agencies, clinical trial registries, and the websites of relevant associations. Relevant literature, published and unpublished, was selected by two reviewers working independently. Randomized controlled trials (RCTs) were selected and assessed for study design quality (Jadad scale) and information on the following were abstracted: deaths, serious or life threatening adverse events, COPD exacerbations, upper respiratory tract infections (URTIs) during treatment, hospitalizations during treatment, rescue short-acting ß 2-agonist use for acute symptomatic relief, symptom-free days, dyspnea, lung function tests, walk tests, and quality of life measures. Trials were included if they compared long-acting ß 2-agonists (salmeterol or formoterol) with placebo or with an anticholinergic agent (ipratropium or tiotropium), with or without short-acting inhaled ß 2-agonists on an as-needed basis. Meta-analyses of long-acting ß 2-agonists versus placebo, and long-acting ß 2-agonists versus anticholinergics were performed.

Further research/reviews required

There is an urgent need for experts to set internationally accepted standards for outcome measures in COPD drug trials and establish a minimum number of objective outcome measures to prove the efficacy and effectiveness of these drugs.

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