Aclidinium bromide: clinical benefit in patients with moderate to severe COPD
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CRD summary
The author concluded that aclidinium bromide had at least similar outcomes to those of other long-acting bronchodilators. The review process had major limitations, and the opportunity for bias in the included trials was unknown. The larger trials were placebo controlled, with little direct evidence comparing aclidinium bromide and other bronchodilators. The conclusions of the review may not be reliable.

Authors' objectives
To provide an overview of clinical studies evaluating the safety and efficacy of inhaled aclidinium bromide (a long-acting anticholinergic bronchodilator) for chronic obstructive pulmonary disease (COPD).

Searching
PubMed, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to October 2012; search terms were reported. ClinicalTrials.gov was searched. The searches were limited to full-text articles, published in English in peer-reviewed journals.

Study selection
Eligible studies were randomised controlled trials (RCTs) of inhaled aclidinium bromide, compared with placebo, tiotropium bromide, indacaterol, salmeterol, formoterol, or glycopyrronium bromide. Trials had to be of adults aged over 40 years, with stable moderate-to-severe COPD. The outcomes of interest included the onset of action, various measures of the forced expiratory volume in one second (FEV1), exercise capacity, health status, symptom relief, use of rescue medication, and exacerbations.

In the included trials, the mean age of the participants ranged from 58 to 65 years. Their baseline FEV1 ranged from 43% to 56% of the predicted value, and their smoking history ranged from 39 to 58 pack-years. The most common dose of aclidinium bromide was 200 micrograms.

It appears that one reviewer selected studies for inclusion.

Assessment of study quality
The author did not report that trial quality was assessed.

Data extraction
The summary data were extracted to calculate differences between groups. It appears that one reviewer extracted the data.

Methods of synthesis
A narrative synthesis was presented.

Results of the review
Ten RCTs (3,922 participants; range 17 to 843) were included in the review; all were multicentre RCTs sponsored by a single pharmaceutical company. The control was placebo in six RCTs, tiotropium bromide plus placebo in three RCTs, and formoterol in one RCT. The length of trials, where reported, ranged from one to 52 weeks.

Aclidinium bromide had clinically important effects on the FEV1 (four RCTs), health status (three RCTs), use of relief medication (two RCTs), and daytime dyspnoea scores (two RCTs).

The treatment effect of aclidinium bromide on exercise tolerance, as measured by exercise endurance time, in one trial, appeared to be at least comparable to that of other long-acting bronchodilators. Three trials reported mixed results for the effects of aclidinium bromide on exacerbations. One trial reported cardiac and vascular disorders at a similar frequency, in both the intervention and control groups.
Authors' conclusions
The effects of aclidinium bromide on relevant COPD outcomes were at least similar to those of other long-acting bronchodilators; it could have a significant role in the management of moderate-to-severe COPD.

CRD commentary
The review question and inclusion criteria were clear. Relevant sources were searched. Language restrictions were applied and the search was limited to full-text published articles; language bias may have been present and some trials may have been missed. It was unclear whether trial selection and data extraction were carried out with sufficient attempts to minimise error and bias.

The absence of any formal quality assessment for the included trials, limits the interpretation of the reliability of the findings. The trial details were provided. A narrative synthesis was appropriate as there were insufficient data to pool in a meta-analysis.

There were significant limitations in the review process, and the opportunity for bias in the included trials was unknown. Most of the larger trials were placebo controlled, with little evidence from direct comparisons between aclidinium bromide and other bronchodilators. The conclusions of the review may not be reliable.

Implications of the review for practice and research
Practice: The author did not state any implications for practice.

Research: The author stated that long-term controlled trials, with the exacerbation rate as the primary outcome, were needed to explore the effects of aclidinium bromide on the COPD exacerbation rate. Trials were also needed to determine whether twice-daily dosing with aclidinium bromide had a clinically important effect on nighttime symptom scores.

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**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.