Tiotropium versus long-acting beta-agonists for stable chronic obstructive pulmonary disease (Review)

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Tiotropium versus long-acting beta-agonists for stable chronic obstructive pulmonary disease

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ABSTRACT

Background

Tiotropium and long-acting beta₂-agonists (LABAs) are both accepted in the routine management for people with stable chronic obstructive pulmonary disease (COPD). There are new studies which have compared tiotropium with LABAs, including some that have evaluated recently introduced LABAs.

Objectives

To compare the relative clinical effects of tiotropium bromide alone versus LABA alone, upon measures of quality of life, exacerbations, lung function and serious adverse events, in people with stable COPD.

To critically appraise and summarise current evidence on the costs and cost-effectiveness associated with tiotropium compared to LABA in people with COPD.

Search methods

We identified randomised controlled trials (RCTs) from the Cochrane Airways Group Specialised Register of trials and economic evaluations from searching NHS EED and HEED (date of last search February 2012). We found additional trials from web-based clinical trial registers.

Selection criteria

We included RCTs and full economic evaluations if they compared effects of tiotropium alone with LABAs alone in people with COPD.

We allowed co-administration of standard COPD therapy.

Data collection and analysis

Two review authors independently assessed studies for inclusion, then extracted data on study quality and outcomes. We contacted study authors and trial sponsors for additional information. We analysed data using the Cochrane Review Manager (RevMan 5.1) software.
Main results

Seven clinical studies totalling 12,223 participants with COPD were included in the review. The studies used similar designs and were generally of good methodological quality. Inclusion criteria for RCTs were similar across the included studies, although studies varied in terms of smoking history and COPD severity of participants. They compared tiotropium (which was delivered by HandiHaler in all studies) with salmeterol (four studies, 8936 participants), formoterol (one study, 431 participants) and indacaterol (two studies, 2856 participants). All participants were instructed to discontinue anticholinergic or long-acting beta-agonist bronchodilators during treatment, but could receive inhaled corticosteroids (ICS) at a stable dose. Study duration ranged from 3 to 12 months. We extracted data for 11,223 participants. In general, the treatment groups were well matched at baseline. Overall, the risk of bias across the included RCTs was low.

In the analysis of the primary outcomes in this review, a high level of heterogeneity amongst studies meant that we did not pool data for St George's Respiratory Questionnaire quality of life score. Subgroup analyses based on the type of LABA found statistically significant differences among effects on quality of life depending on whether tiotropium was compared with salmeterol, formoterol or indacaterol. Tiotropium reduced the number of participants experiencing one or more exacerbations compared with LABA (odds ratio (OR) 0.86; 95% confidence interval (CI) 0.79 to 0.93). For this outcome, there was no difference seen among the different types of LABA. There was no statistical difference in mortality observed between the treatment groups.

For secondary outcomes, tiotropium was associated with a reduction in the number of COPD exacerbations leading to hospitalisation compared with LABA treatment (OR 0.87; 95% 0.77 to 0.99), but not in the overall rate of all-cause hospitalisations. There was no statistically significant difference in forced expiratory volume in one second (FEV1) or symptom score between tiotropium and LABA-treated participants. There was a lower rate of non-fatal serious adverse events recorded with tiotropium compared with LABA (OR 0.88; 95% CI 0.78 to 0.99). The tiotropium group was also associated with a lower rate of study withdrawals (OR 0.89; 95% CI 0.81 to 0.99).

We identified six full economic evaluations assessing the cost and cost-effectiveness of tiotropium and salmeterol. The studies were based on an economic model or empirical analysis of clinical data from RCTs. They all looked at maintenance costs and the costs for COPD exacerbations, including respiratory medications and hospitalisations. The setting for the evaluations was primary and secondary care in the UK, Greece, Netherlands, Spain and USA. All the studies estimated tiotropium to be superior to salmeterol based on better clinical outcomes (exacerbations or quality of life) and/or lower total costs. However, the authors of all evaluations reported there was substantial uncertainty around the results.

Authors’ conclusions

In people with COPD, the evidence is equivocal as to whether or not tiotropium offers greater benefit than LABAs in improving quality of life; however, this is complicated by differences in effect among the LABA types. Tiotropium was more effective than LABAs as a group in preventing COPD exacerbations and disease-related hospitalisations, although there were no statistical differences between groups in overall hospitalisation rates or mortality during the study periods. There were fewer serious adverse events and study withdrawals recorded with tiotropium compared with LABAs. Symptom improvement and changes in lung function were similar between the treatment groups. Given the small number of studies to date, with high levels of heterogeneity among them, one approach may be to give a COPD patient a substantial trial of tiotropium, followed by a LABA (or vice versa), then to continue prescribing the long-acting bronchodilator that the patient prefers. Further studies are needed to compare tiotropium with different LABAs, which are currently ongoing. The available economic evidence indicates that tiotropium may be cost-effective compared with salmeterol in several specific settings, but there is considerable uncertainty around this finding.

Plain language summary

Tiotropium versus long-acting beta₂-agonists (LABAs) in the management of COPD

Tiotropium is an inhaled medication that helps open the airways (bronchodilator) and is used to manage persistent symptoms of COPD. We found seven studies including 12,223 participants that compared tiotropium with long-acting beta₂-agonists (LABAs), which are another type of bronchodilator. This systematic review found that currently there is insufficient evidence to suggest which of these treatments provides greater long-term benefit in quality of life. Furthermore, both treatments had similar effects on symptoms, lung function and death rates.
Tiotropium appears better than LABAs in preventing COPD exacerbations (worsening of COPD symptoms) and reducing the number of COPD-related hospitalisations. Furthermore, there were fewer participants during the study period with serious adverse events or who withdrew early from the studies with tiotropium compared with LABA treatment. However, there was no difference in the total number of people who were hospitalised.

We found six economic evaluations looking at the cost and effectiveness of tiotropium and the LABA salmeterol that were conducted in the UK, Greece, Netherlands, Spain, or USA. All the studies estimated tiotropium to be better than salmeterol based on medical outcomes (exacerbations or quality of life) and/or lower total costs, including respiratory medications and hospitalisations. However, these results were very uncertain.