Effect of tiotropium on quality of life in COPD: a systematic review
Kaplan A

CRD summary
The author concluded that tiotropium improved the quality of life for patients with chronic obstructive pulmonary disease who required long-acting bronchodilator treatment. Given the unclear quality of included trials, the small number of trials and the absence of clinically significant differences for many trials, the author's conclusions should be treated with caution.

Authors' objectives
To assess the impact of long-acting anticholinergic tiotropium on health related quality of life in patients with chronic obstructive pulmonary disease (COPD).

Searching
PubMed, EMBASE and BIOSIS Previews were searched for articles published in English from 1990 to 2009. Search terms were reported.

Study selection
Double-blind randomised controlled trials (RCTs) that compared tiotropium with placebo or active comparators in patients with a diagnosis of COPD were eligible for inclusion. Eligible patients were required to have a smoking history of 10 pack years or more. Trials had to report health-related quality of life outcomes. Secondary analyses of trials were permitted if they produced new data.

Included trials compared tiotropium 18μg once daily monotherapy versus placebo or other active agents (budesonide fluticasone, formoterol, ipratropium, salmeterol or salmeterol plus fluticasone propionate) with or without tiotropium. The duration of included trials ranged from 42 days to four years. The mean baseline dyspnoea index ranged from 5.7 to 7.41 (where stated). Outcomes reported in the review were quality of life measured by the St Georges Respiratory Questionnaire (SGRQ), the Transition Dyspnoea Index (TDI) and/or the Short Form 36 (SF-36).

The author did not state how the studies were selected for the review or how many reviewers performed the study selection.

Assessment of study quality
The author did not state that they assessed trial quality.

Data extraction
The main findings for each trial were extracted.

The author did not state how the data extraction was performed.

Methods of synthesis
The results were combined in a narrative synthesis and grouped according to comparator. The findings were also judged as to their clinical significance.

Results of the review
Twenty-four publications were included for review. There were 16 double-blind RCTs (n=13,584 patients) plus four secondary analyses (from two of the included RCTs) and four subgroup analyses (from two of the included RCTs).

Tiotropium versus placebo (nine RCTs; four secondary analyses and four subgroup analyses; n=10,291)

Eight trials of primary data compared tiotropium with placebo on the St Georges Respiratory Questionnaire (SGRQ). Six trials reported statistically significant benefits with tiotropium (p-values ranged from <0.05 to <0.001). The differences between tiotropium and placebo were clinically meaningful in only two of these trials. However,
significantly more patients who received tiotropium achieved clinically significant change compared with patients who received placebo in five trials (p<0.05 to p<0.001). Subgroup analyses revealed that statistically and clinically significant benefits were observed with tiotropium compared with placebo in GOLD stage II patients, patients who did not receive maintenance therapy at baseline and patients who smoked. Five trials of primary data compared tiotropium with placebo on the Transition Dyspnoea Index (TDI). Three reported statistically and clinically significant benefits with tiotropium (p=0.03 to p<0.001). Tiotropium significantly improved physical but not mental health domains on the Short Form 36 (SF-36; one trial; p<0.05).

Tiotropium versus active comparators (eight RCTs; n=4,500)

Tiotropium showed significant benefits as measured on SGRQ compared with ipratropium (one trial; n=535; p=0.004) and salmeterol (one trial; n=1,207; p<0.01). However, tiotropium showed significantly less improvement on the SGRQ compared with salmeterol plus fluticasone (one trial; n=1,323; p=0.038). Tiotropium was superior to ipratropium (p<0.05) but not salmeterol in improving TDI scores. Tiotropium dual therapy with salmeterol significantly improved SGRQ scores (one trial; p=0.02), but not TDI scores compared with tiotropium alone. Two trials (n=285) evaluated tiotropium combined with formoterol; in one trial TDI scores significantly improved (p=0.0002), but SGRQ scores did not compared with tiotropium monotherapy. Tiotropium triple therapy (three trial; n=1,150) significantly improved SGRQ scores in two trials compared with tiotropium monotherapy (p=0.02 and 0.023) and significantly improved TDI scores in one trial (p<0.001).

Authors’ conclusions

Tiotropium improved the quality of life for patients with chronic obstructive pulmonary disease who required long-acting bronchodilator treatment. Other additional therapies provided further benefits depending on the population.

CRD commentary

The review addressed a clear question with well-defined inclusion criteria. Three relevant databases were searched, but the search was restricted to articles in English and did not appear to include unpublished material, so language and publication bias could not be ruled out. It was unclear whether suitable steps were taken to minimise the risk of reviewer error or bias in the study selection and data extraction stages of the review.

Only double blind RCTs were included in the review, but the quality of these trials was not assessed, so the reliability of the findings was unclear. Given the wide range of comparator conditions, the decision to combine the trials in a narrative synthesis was appropriate. The authors considered the clinical and statistical significance of their findings. However, there were only a small number of trials for each active comparator condition, which made it difficult to draw firm conclusions. Quality of life was the primary endpoint in only one of the included trials.

In light of the unclear quality of included trials, the small number of trials and the absence of clinically significant differences for many trials, the author’s conclusions should be treated with caution.

Implications of the review for practice and research

Practice: The author stated that there was a need for a validated and short patient-reported outcome measure for use in clinical practice to quantify the impact of COPD on quality of life.

Research: The author stated that further research was needed to evaluate the impact of tiotropium on health-related quality of life in patients with earlier disease, patients who had not previously received maintenance therapy, and patients who were continuing smokers.

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