A meta-analysis on the efficacy of oral theophylline in patients with stable COPD

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CRD summary
The authors concluded that oral theophylline improved both trough and peak forced expiratory volume and forced vital capacity in patients with stable chronic obstructive pulmonary disease. Given the methodological limitations of the review, and the unknown quality of the included trials, the authors’ conclusions may not be reliable.

Authors' objectives
To evaluate the efficacy of oral theophylline in patients with stable chronic obstructive pulmonary disease (COPD).

Searching
PubMed was searched for English language publications up to June 2005. Search terms were reported. References from relevant systematic reviews were also checked for additional studies.

Study selection
Randomised controlled trials (RCTs) that compared oral theophylline versus placebo in patients with stable chronic obstructive pulmonary disease were eligible for inclusion in the review. Eligible trials had to include participants who had pulmonary function tests before and after treatment. Specific outcomes of interest were trough (pre-dose) and peak (post-dose) forced expiratory volume in one second and/or forced vital capacity.

Where reported, the mean age of the included participants ranged from 58 to 68 years and the majority were male. Baseline forced expiratory volume in one second ranged from 0.77 to 1.37 litres (L). Details of theophylline dosages were provided; duration of treatment ranged from a single dose to three months. The studies included crossover RCTs.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Data were extracted from text, tables and/or graphs. In trials where trough and peak measurements were not differentiated, the difference was determined using the time that the last dose of theophylline was taken and the time that the pulmonary function test was measured.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Meta-analyses examining pooled weighted mean differences with 95% confidence intervals were performed using a fixed effect model.

Results of the review
Eighteen randomised controlled trials (RCTs) were included in the review (n=1,161 participants). Sample sizes ranged from 10 to 854.

Theophylline demonstrated a significant improvement over placebo for trough forced expiratory volume in one second (weighted mean difference 0.108 L, 95% confidence interval (CI): 0.05 to 0.16; 10 RCTs, n=704 patients), trough forced vital capacity (weighted mean difference 0.186 L, 95% CI: 0.04 to 0.34; six RCTs, n=166 patients), peak forced expiratory volume in one second (weighted mean difference 0.096 L, 95% CI: 0.04 to 0.15; 12 RCTs, n=800 patients), and peak forced vital capacity (weighted mean difference 0.242 L, 95% CI: 0.11 to 0.37;10 RCTs, n=358 patients).
Authors' conclusions
Oral theophylline improved both trough and peak forced expiratory volume and forced vital capacity in patients with stable chronic obstructive pulmonary disease.

CRD commentary
The review addressed a clear question. It supported by appropriate inclusion criteria, but trials may have been included that did not meet the a priori criteria. The authors restricted the search to English language publications, introducing the potential for language and publication biases, so some trials may have been missed. Validity was not assessed, making it difficult to assess the reliability of the data. As cross-over trials were included, it is important to ensure that they have been appropriately analysed so that the potential for cross-over effects has been considered. The number of reviewers involved in the systematic review process was not reported, potentially introducing reviewer bias. Details of the included trials were reported. Heterogeneity was not reported, although forest plots were presented. Given the methodological limitations of the review, and the unknown quality of the included trials, the authors' conclusions may not be reliable.

Implications of the review for practice and research
Practice: The authors stated that theophylline remains a third choice in the treatment of chronic obstructive pulmonary disease.

Research: The authors did not state any implications for research.

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