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The effect of low-dose corticosteroids and theophylline on the risk of acute exacerbations of COPD: the TASCS randomised controlled trial

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ABSTRACT

Background: The highest burden of chronic obstructive pulmonary disease (COPD) occurs in low- and middle-income countries. Low-cost oral medications, if effective, could enable affordable, accessible COPD treatment.

Methods: In this randomised, three-arm, double-blind, double-dummy, placebo-controlled study conducted in 37 centres in China, symptomatic patients with moderate to very severe COPD were randomised 1:1:1 to placebo twice daily plus placebo once daily, low-dose theophylline 100 mg twice daily plus placebo once daily or low-dose theophylline 100 mg twice daily plus low-dose oral prednisone 5 mg once daily for 48 weeks. The primary end-point was annualised exacerbation rate.

Results: 1670 subjects were randomised and 1242 completed the study (1142 with acceptable data at week 48). Subjects (75.7% male) had a mean age of 64.4 years, with mean±SD baseline post-bronchodilator forced expiratory volume in 1 s (FEV_1) 1.1±0.4 L (42.2% predicted) and St George's Respiratory Questionnaire (SGRQ) score 45.8±20.1. There were negligible differences between annualised exacerbation rates across the three treatments: 0.89 (95% CI 0.78–1.02) on theophylline plus prednisone, 0.86 (95% CI 0.75–0.99) on theophylline plus placebo and 1.00 (95% CI 0.87–1.14) on placebo. The rate ratio for theophylline plus prednisone *versus* pooled theophylline plus placebo and placebo was 0.96 (95% CI 0.83–1.12), for theophylline plus placebo *versus* placebo was 0.87 (95% CI 0.73–1.03; p=0.101) and for theophylline plus prednisone *versus* placebo was 0.90 (95% CI 0.76–1.06; p=0.201). Secondary outcomes of hospitalisations, FEV_1, SGRQ and COPD Assessment Test score showed no statistically significant difference between treatment arms. Serious adverse events other than exacerbations were <2% and did not differ between treatment arms.

Conclusions: Low-dose theophylline alone or in combination with prednisone did not reduce exacerbation rates or clinically important secondary end-points compared with placebo.