**Study Overview**

**Objective.** To determine the efficacy of oral prednisone in the treatment of outpatients with chronic obstructive pulmonary disease (COPD) exacerbations.

**Design.** Randomized, double-blind, placebo-controlled trial.

**Setting and participants.** 147 patients older than 35 years were recruited from the emergency departments (EDs) of 10 Canadian hospitals after being evaluated and discharged from the ED with a diagnosis of COPD exacerbation.

**Intervention.** The participants were randomized to either 10 days of oral prednisone (40 mg once daily) or identical placebo capsules. All patients received 10 days of oral broad-spectrum antibiotics (ie, 160 mg trimethoprim plus 800 mg sulfamethoxazole twice daily or 100 mg doxycycline twice daily if allergic to sulfa drugs) as well as inhaled albuterol and ipratropium bromide.

**Main outcome measures.** The primary outcome was a return visit to an ED or unscheduled visit to a physician’s office for worsening dyspnea within 30 days of randomization. Secondary outcomes included changes in forced expiratory volume in 1 second (FEV₁), severity of dyspnea, and disease-specific quality of life.

**Main results.** Patients receiving oral prednisone were significantly less likely than placebo recipients to experience relapse at 30 days (27% versus 43%; P = 0.05). Prednisone treatment resulted in improved FEV₁ (absolute increase, 0.16 liter; P = 0.007) as well as significantly improved dyspnea as defined by a standard dyspnea index (P = 0.04). However, there was no difference between treatment assignments in the overall quality of life score as measured by the Chronic Respiratory Disease Index Questionnaire (P = 0.14). Side effects including increased appetite, weight gain, and insomnia were more common among patients receiving prednisone.

**Conclusion.** Outpatient treatment of COPD exacerbations with oral prednisone is effective at reducing return visits and improving lung function; however, overall quality of life is unchanged, likely secondary to an increased incidence of side effects.

**Commentary**

COPD remains a major public health concern in the United States, affecting 16 million people and ranking fourth as a leading cause of death. Moreover, COPD is responsible for over 16 million office visits per year, with direct health care costs in 1995 estimated to be more than $14 billion [1]. New therapies aimed at the treatment of acute exacerbations are of particular importance as typical patients will experience a median of 2 to 3 exacerbations per year [2].

Previous work has demonstrated that a combination of intravenous and oral systemic corticosteroids among inpatients with acute COPD exacerbations results in reduced rates of treatment failure and length of hospitalization [3]. However, studies evaluating the use of systemic corticosteroids in outpatients with acute exacerbations have been limited, leading to some conflict in guideline recommendations regarding the use of oral corticosteroids for outpatients [4].

The current study by Aaron et al provides extremely relevant information in the management of obstructive lung disease. By selecting patients with known COPD and evidence of an acute exacerbation and carefully excluding those with evidence of asthma or reversible airflow obstruction, the authors have isolated patients for whom the absolute risks and benefits of outpatient corticosteroids were previously unclear. While there was no reduction in hospitalization rates, the reduction of recurrent office visits is certainly an important finding for both patients and providers. In addition, patients reported significant improvement in dyspnea symptoms related to their acute exacerbation.

Despite the positive findings of this study, many questions remain. Patients reported significant increases in multiple known side effects of corticosteroids, including weight...
gain and insomnia, which possibly contributed to the lack of improvement in overall quality of life. It is important to note that patients with uncontrolled diabetes were excluded from this intervention, and careful monitoring of glycemic control was not undertaken among enrolled diabetics. As a result, it is difficult to comment on the incidence of hyperglycemia, which has been reported in other trials [3]. In addition, questions remain surrounding the optimal length of therapy, especially in light of the fact that multiple courses of corticosteroids will likely be needed, with possible long-term risks including osteoporosis, glucose intolerance, and hypertension.

Applications for Clinical Care

A 10-day course of oral prednisone (40 mg/day) appears to be beneficial in reducing recurrent visits and improving dyspnea for outpatients with COPD exacerbations. However, these benefits need to be weighed against side effects of corticosteroids including weight gain, insomnia, and possible hyperglycemia in diabetics.

—Review by Thomas D. Sequist, MD

References