Withdrawing Systemic Corticosteroids in Patients with COPD

Rice KL, Rubins JB, Lebahn F, Parenti CM, Duane PG, Kuskowski M, et al. Withdrawal of chronic systemic corticosteroids in patients with COPD. A randomized trial. Am J Respir Crit Care Med 2000;162:174–8.

Study Overview

Objective. To determine whether patients with "steroid-dependent" chronic obstructive pulmonary disease (COPD) can be tapered off long-term oral corticosteroid treatment.

Design. Randomized, double-blind, placebo controlled trial. Analysis was by intention to treat.

Setting and participants. Using computerized pharmacy data from a single Veterans Affairs Medical Center, 164 potential subjects were invited by mail to participate if they had received β agonists and ≥ 5 mg/day of oral prednisone for the preceding 6 months without a dosage reduction in the previous month. All 164 patients were at least 50 years old, smoked at least 20 pack-years, and met the American Thoracic Society's criteria for COPD. Study patients did not meet any of the exclusion criteria: a clinical diagnosis of asthma, history of eosinophilia, high IgE titer, family history of atopy, concomitant major illness limiting travel, or 6-month life expectancy. 122 patients declined to participate because of an unwillingness to discontinue chronic prednisone (24 patients), logistical problems (42 patients), or an unstated reason (56 patients). Four individuals dropped out of a 1-week run-in phase, during which all subjects received their regular dose of prednisone in the study preparation. The remaining 38 patients were men, with a mean ± SD age of 70 ± 7 years and a baseline forced expiratory volume in 1 second (FEV_1) of 0.96 ± 0.44 L, and were receiving 11.1 ± 5.3 mg/day of prednisone.

Intervention. Patients were randomly assigned either to the "demand" group (daily prednisone dose decreased by 5 mg each week, n = 18) or to the "continuous" group (received usual maintenance dose throughout study, n = 20). All doses were given in identical-appearing capsule preparations. For exacerbations (which were treated on an outpatient basis), both groups received 40 mg/day of open-label oral prednisone for 10 days. Hospitalized patients received parenteral corticosteroids at their physician's discretion and then completed the remainder of a 10-day course of prednisone (40 mg/day) after discharge. All patients took 1600 g of inhaled triamcinolone acetonide daily, in divided doses.

Main outcome measures. The average number of COPD exacerbations. Exacerbations were defined prior to the start of the study. Secondary outcome measures included average daily systemic corticosteroid dose (including all oral and parenteral doses), dyspnea index, and health-related quality of life as assessed by the Medical Outcomes Study Short Form-36.

Main results. Twelve (60%) continuous-group and 8 (44%) demand-group patients took the study preparation throughout the 6-month study period (P = 0.34). The continuous group used a mean of 10.7 ± 5.2 mg/day of systemic corticosteroids, while the demand group used 6.3 ± 6.4 mg/day (P = 0.003). The continuous group experienced a mean ± SD of 2.5 ± 2.7 exacerbations compared with 2.7 ± 2.5 in the demand group (P = 0.60). Dyspnea index and quality-of-life scores did not differ between groups or from beginning to end of the study. The demand group lost a mean 4.8 ± 2.0 kg from baseline to 6 months; the continuous group gained 0.5 ± 3.5 kg (P = 0.007).

Conclusion

Preliminary data suggest that some COPD patients who are considered to be "steroid-dependent" may safely taper off their systemic corticosteroids without a decrement in symptom scores or quality of life.

Commentary

Rice and colleagues designed a very elegant study. They included a run-in period to assess patient compliance with the study preparation and questionnaires to determine whether the study allocation remained concealed to the patients (it did) and the study coordinator (who correctly guessed 80% of the patients' assignments). Although half of patients stopped taking the study preparation (after a mean 129 ± 60 days [continuous] and 103 ± 62 days [demand]; P = 0.15), the intervention had the desired effect of decreasing the average daily dose of systemic corticosteroids.

There were 2 primary weaknesses in this study. Less than a quarter of the invited patients participated, strongly suggesting selection bias. If some or most of these patients had unsuccessfully tried to taper off their prednisone and therefore

declined participation, this may have substantially biased the results toward no difference between groups. Also, the small number of subjects and relatively brief follow-up did not allow investigators to assess the long-term risks or potential benefits of decreasing systemic corticosteroids.

Applications for Clinical Practice

This study highlights the paucity of definitive evidence regarding the benefits and risks of systemic corticosteroids for COPD patients who do not have asthma. While good published evidence suggests short-term benefits from short-term systemic corticosteroid use [1], we have minimal peer-reviewed data on long-term treatment. A randomized controlled trial by Renkema et al [2] showed no benefit from adding systemic to inhaled corticosteroids. Given the serious side effects of systemic corticosteroids, practitioners should consider a trial dose reduction for all of their "steroid-dependent" COPD patients. More conclusive evidence on systemic corticosteroids and their use in COPD therapy will come with much larger and longer trials.

References

1. Niewoehner DE, Erbland ML, Deupree RH, Collins D, Gross NJ, Light RW, et al. Effect of systemic glucocorticoids on exacerbations of chronic obstructive pulmonary disease. Department of Veterans Affairs Cooperative Study Group. N Engl J Med 1999;340:1941–7.
2. Renkema TE, Schouten JP, Koeter GH, Postma DS. Effects of long-term treatment with corticosteroids in COPD. Chest 1996;109:1156–62.