

Glucocorticoids reduced short-term treatment failure in exacerbations of chronic obstructive pulmonary disease

Niewoehner DE, Erbland ML, Deupree RH, et al., for the Department of Veterans Affairs Cooperative Study Group. Effect of systemic glucocorticoids on exacerbations of chronic obstructive pulmonary disease. *N Engl J Med.* 1999 Jun 24;340:1941-7.

QUESTION

In patients who are hospitalized with exacerbations of chronic obstructive pulmonary disease (COPD), do glucocorticoids reduce the rate of first treatment failure?

DESIGN

Randomized (allocation concealed*), blinded (clinicians and patients),* placebo-controlled trial with follow-up at 1, 3, and 6 months.

SETTING

25 U.S. Veterans Affairs medical centers.

PATIENTS

271 patients (mean age 68 y, 99% men, 83% white) hospitalized with COPD. Inclusion criteria were age ≥ 50 years, history of ≥ 30 pack-years of smoking, and FEV₁ ≤ 1.5 L or inability to have spirometry because of dyspnea. Exclusion criteria were asthma, recent use of study drugs, or expected survival < 1 year.

INTERVENTION

Patients received broad-spectrum antibiotics for 1 week and inhaled β -adrenergic agonist, ipratropium bromide, and triamcinolone acetonide for 6 months. Medications other than study drugs could be

used. Patients were allocated to either 8 or 2 weeks of therapy ($n = 80$ each) or to placebo ($n = 111$). 8-week therapy was intravenous methylprednisolone, 125 mg every 4 hours for 72 hours, and then oral prednisone, 60 mg/d with tapering to day 57. The 2-week therapy was identical except that tapering stopped at day 15.

MAIN OUTCOME MEASURE

First treatment failure (death, need for intubation and mechanical ventilation, readmission for COPD, or intensification of drug therapy).

MAIN RESULTS

Data from the active drug groups were combined because 8-week treatment was not superior to 2-week treatment. The rate of treatment failure was lower in the active drug groups than in the placebo group at 1 month and 3 months (Table) ($P = 0.04$ for both groups using the log-

rank test [survival data]) but not at 6 months (51% vs 54%, $P = 0.6$). Patients in the active drug groups spent fewer days in the hospital (8.5 vs 9.7 d, $P = 0.03$) and had a higher FEV₁ at days 1, 2, and 3 ($P < 0.05$). Mortality rates did not differ (8.1% vs 9.9%, $P = 0.6$). Hyperglycemia severe enough to warrant treatment was higher in the active drug group (15% vs 4%, $P = 0.002$).

CONCLUSION

Systemic glucocorticoids reduced the rate of first treatment failure in patients hospitalized with exacerbations of COPD.

Source of funding: Department of Veterans Affairs Cooperative Studies Program.

For correspondence: Dr. D.E. Niewoehner, Pulmonary Section (111N), Veterans Affairs Medical Center, 1 Veterans Drive, Minneapolis, MN 55417, USA. FAX 612-727-5634. ■

*See Glossary.

Treatment failure for systemic glucocorticoids vs placebo for exacerbations of chronic obstructive pulmonary disease†

Time	Glucocorticoids	Placebo	RRR (95% CI)‡	NNT (CI)
1 mo	23%	33%	31% (-2 to 53)	10 (5 to infinity)
3 mo	37%	48%	23% (-3 to 42)	9 (4 to infinity)

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

‡Point estimates somewhat underestimate the survival analysis reported in the article and abstract text.

COMMENTARY

Clinicians frequently use systemic corticosteroids to treat exacerbations of COPD. The underlying evidence has been modest, and guidelines have given only qualified support (1). A study by Davies and colleagues (2) and this study by Niewoehner and colleagues change this by showing a clinically important benefit from systemic corticosteroids in exacerbations of COPD. Both trials reduced hospital stay by about 2 days. Niewoehner and colleagues found that corticosteroids reduced first treatment failure. Davies and colleagues showed a benefit with a lower daily steroid dose (30 mg) than that of Niewoehner and colleagues (60 mg). 2 weeks of therapy was beneficial, whereas 8 weeks was not necessarily better.

Both studies showed an improvement in airway obstruction, which could occur by direct effects on mucosal edema, mucus secretion, or airway inflammatory cells. This finding implies that corticosteroid-responsive airway inflammation may occur in exacerbations of COPD.

Other issues relating to the use of corticosteroids for exacerbations of COPD need clarification: What route? For how long? Should therapy be tapered or stopped abruptly? Similar issues

surround the use of corticosteroids for exacerbations of asthma, and in general, a simple oral regimen is adequate, usually 30 to 50 mg/d abruptly ceasing after 14 days.

The treatment is not without risk. Patients with COPD who received systemic glucocorticoids had increased hyperglycemia. Other studies have shown increased risks for secondary infections, cataracts, vertebral fractures, and myopathies (3). Clinicians can be reassured in their continued use of oral prednisone for exacerbations of COPD. Evidence about stopping may be just as important as evidence about starting.

Peter G. Gibson, MBBS
John Hunter Hospital
Newcastle, New South Wales, Australia

References

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3. McEvoy CE, Niewoehner DE. *Chest.* 1997;111:732-43.