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


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

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

Setting
25 US Veterans Affairs medical centres.

Patients
271 patients (mean age 68 y, 99% men, 83% white) admitted to hospital 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 dyspnoea. 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 treatment (n = 80 each) or to placebo (n = 111). 8-week treatment was intravenous methylprednisolone, 125 mg every 4 hours for 72 hours, and then oral prednisone, 60 mg/day with tapering to day 57. The 2-week treatment 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% v 54%, p = 0.6). Patients in the active drug groups spent fewer days in the hospital (8.5 v 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% v 9.9%, p = 0.6). Hyperglycaemia severe enough to warrant treatment was higher in the active drug group (15% v 4%, p = 0.0002).

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

*See glossary.

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 colleagues2 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 (50 mg) than that of Niewoehner and colleagues (60 mg). 2 weeks of treatment 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 treatment 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/day abruptly ceasing after 14 days.

The treatment is not without risk. Patients with COPD who received systemic glucocorticoids had increased hyperglycaemia. 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.

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

<table>
<thead>
<tr>
<th>Time</th>
<th>Glucocorticoids</th>
<th>Placebo</th>
<th>RRR (95% CI)‡</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>23%</td>
<td>33%</td>
<td>31% (2 to 53)</td>
<td>10 (5 to infinity)</td>
</tr>
<tr>
<td>3 month</td>
<td>37%</td>
<td>48%</td>
<td>23% (3 to 42)</td>
<td>9 (4 to infinity)</td>
</tr>
</tbody>
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†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.