Priority Updates from the Research Literature from the Family Physicians Inquiries Network

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Steroids for acute COPD—but for how long?

Not only was a shorter course of glucocorticoid therapy as effective as a 14-day regimen, but there was no difference in the time to next exacerbation.

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PRACTICE CHANGER

Prescribe a 5-day regimen of glucocorticoid therapy for acute chronic obstructive pulmonary disease (COPD) exacerbations; the shorter course of treatment appears to be as effective as a 14-day regimen.[1]

STRENGTH OF RECOMMENDATION

B: Based on a single well-done randomized controlled trial (RCT).

Leuppi JD, Schuetz P, Bingisser R, et al. Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial. *JAMA*. 2013;309:2223-2231.

ILLUSTRATIVE CASE

A 55-year-old man with COPD presents to the emergency department (ED) because of progressive shortness of breath, cough, and sputum production over the past 4 days. He is diagnosed with a COPD exacerbation, treated with corticosteroids, and admitted to the hospital. His inpatient treatment includes antibiotics, inhaled albuterol and ipratropium, supplemental oxygen, and oral corticosteroids.

How many days should he take oral steroids?

Severe exacerbations of COPD are independently associated with mortality,[2] regardless of baseline severity. Guidelines and systematic reviews highlight the importance of using oral glucocorticoids in the management of acute COPD exacerbations, as the drugs have been found to shorten recovery time and length of hospital stay, improve lung function, and reduce the risk of early relapse and treatment failure.[3-5] What is not clear is how long the course of oral steroids should be.

What we know (and don't know) about duration

Data supporting a 14-day course of steroids vs a longer (8-week) duration comes from the Systemic Corticosteroids in COPD Exacerbations trial.[6] Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria suggest a 10- to-14-day regimen (30-40 mg/d), but acknowledge that there is a lack of data from clinical and observational studies to support this recommendation.[3] A recent Cochrane review compared a short course of treatment (3-7 days) with a longer regimen (10-15 days) and found that the evidence to support a clinical practice change was inconclusive.[5]

The study detailed in this PURL—a double-blind RCT comparing 5-day with 14-day oral steroid treatment in patients hospitalized for acute COPD exacerbation—had more definitive results.[1]

STUDY SUMMARY

Shorter and longer regimens produce equal results

Leuppi et al[1] used noninferiority methodology to compare a 5- vs a 14-day course of prednisone (40 mg/d) to treat patients with

This trial clearly demonstrated that 40 mg prednisone for 5 days is at least as good as a 14-day regimen. What's more, it is not necessary to taper the short-course therapy, which simplifies treatment.

COPD exacerbations. A patient was considered to have a COPD exacerbation if he or she had a change from baseline in ≥2 of the following: dyspnea, cough, sputum quantity, or purulence.

Participants were patients who came to the EDs of 5 Swiss teaching hospitals between March 2006 and February 2011. To be eligible, individuals had to be 40 years or older and have ≥20 pack-years of smoking. Exclusion criteria included asthma, mild obstruction (forced expiratory volume in one second/forced vital capacity >70%), pneumonia, an estimated survival <6 months, pregnancy, and lactation.

All the participants (N=311) received 40 mg methylprednisolone intravenously on Day 1, followed by prednisone 40 mg orally on Days 2 through 5. The researchers then randomly divided participants into 2 groups: One group continued to take prednisone 40 mg/d and the other group received a matching placebo for an additional 9 days. Participants in both groups also received antibiotics for 7 days, twice daily inhaled steroids, daily tiotropium, and nebulized albuterol, as needed; additional oral glucocorticoids could be administered, as well, at the discretion of the treating physicians.

The primary outcome was the time to the next COPD exacerbation, up to 180 days. Noninferiority between the groups was defined as no more than a 15% absolute increase in exacerbations. The dropout rate was 5.7%, evenly divided between groups. Intention to treat and per-protocol analyses were conducted, and hazard ratios (HRs) were calculated using the Kaplan-Meier method and Cox proportional hazards models.

The time to next COPD exacerbation did not differ between the study groups: 56 days for those on the 5-day steroid regimen vs 57 days for those on the 14-day regimen in the intention to treat analysis (HR=0.95; 90% confidence interval, 0.70–1.29; *P*=.006). Sensitivity analyses adjusting for baseline characteristics provided similar results, as did the per-protocol analysis.

Secondary outcomes (overall survival; need for mechanical ventilation; need for additional corticosteroids; and clinical performance measures, such as dyspnea score and quality of life) also did not differ between groups. Nor were there differences in hyperglycemia, worsening hypertension, infection, or other adverse effects typically associated with glucocorticoid use. The active treatment group took >400 mg more prednisone than the placebo group (mean, 793 mg vs 379 mg; *P*<.001).

WHAT'S NEW

Now we know: 5 days is enough

While randomized trials have found that glucocorticoids improve COPD symptoms, the optimal treatment dose and duration were not known. Indeed, current guidelines recommend treatment for >5 days.[3] This trial clearly demonstrated that 40 mg prednisone for 5 days is at least as good as a 14-day treatment course. Furthermore, it is unnecessary to taper the short-course therapy, which simplifies the regimen.

CAVEATS

Will the results apply to those less severely ill?

More than 80% of patients with acute COPD exacerbations can be managed in an outpatient setting.[3] However, participants in this trial were hospitalized for a median of 8.5 days, and most had severe or very severe COPD—and thus, were not fully representative of COPD patients typically seen in an outpatient practice. Yet patients with less severe disease should be at least as likely to respond to short-course steroids as those whose COPD is more severe.

It is important to note that participants in this study all received optimal guideline-based therapies during hospitalization, which may be difficult to achieve for some patients treated in an outpatient setting. Finally, treatment adherence observed during the hospitalization period in this trial is unlikely to be replicated in the outpatient setting.

CHALLENGES TO IMPLEMENTATION

Identifying patients who need steroids for a longer duration

For patients with new COPD exacerbations or those successfully treated using short-course

therapy in the past, a 5-day regimen may be appropriate. For those who have failed prior attempts at short-course treatment, however, a 14-day course of treatment may be more advisable. That said, no guidelines are available to help us determine which of those who were previously treated with a longer regimen may fail on the shorter course of treatment. JFP

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