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This adjunct medication can speed CAP recovery

Adding prednisone to the antibiotic regimen can help patients hospitalized with community-acquired pneumonia to stabilize more quickly and leave the hospital sooner.

PRACTICE CHANGER

Prescribe oral prednisone 50 mg/d to hospitalized patients with mild to moderate community-acquired pneumonia. It decreases time to clinical stability and length of hospital stay.[1]

STRENGTH OF RECOMMENDATION

A: Based on a single good-quality randomized controlled trial and meta-analysis.

Blum CA, Nigro N, Briel M, et al. Adjunct prednisone therapy for patients with community-acquired pneumonia: a multicentre, double-blind, randomized, placebo-controlled trial. *Lancet.* 2015;385:1511-1518.

ILLUSTRATIVE CASE

A 75-year-old woman with hypertension and diabetes mellitus presents to the emergency department with shortness of breath, cough, and fever that she's had for 4 days. On examination, her temperature is 38.2°C (100.7°F), heart rate is 110 beats/min, respiratory rate is 28 breaths/min, oxygen saturation is 91%, and rhonchi are heard in her right lower lung field. A chest x-ray reveals an infiltrate in her right lower lobe. The patient is admitted and started on intravenous (IV) antibiotics, IV fluids, acetaminophen for fever, and oxygen. Can anything else be done to speed her recovery?

Community-acquired pneumonia (CAP) is responsible for more than one million hospitalizations annually in the United States, and is the 8th leading cause of death.[2,3] Treatment of CAP typically consists of antibiotics and supportive measures such as IV fluids and antipyretics. Because the disease process of CAP involves extensive inflammation, adjunct treatment with corticosteroids may be beneficial.

Multiple studies have shown that treatment with corticosteroids can help patients with severe CAP, but the potential benefit in patients with less severe CAP has been uncertain.[4,5] A Cochrane systematic review published in 2011 identified 6 small randomized controlled trials (RCTs) that evaluated the impact of corticosteroids on recovery from CAP.[4] It suggested that corticosteroids may decrease time to recovery, but the studies that included patients with less severe CAP had a relatively high risk of bias.

Subsequently, a 2012 meta-analysis of 9 RCTs explored whether corticosteroids affected mortality in CAP; no benefit was observed in patients with less severe CAP.[5] Most recently, a 2013 meta-analysis of 8 moderate-quality RCTs showed that corticosteroid use was associated with shorter hospital stays, but no change in mortality.[6]

The synthesis of small or moderate-quality studies suggests some potential benefit in treating less severe CAP with corticosteroids, but there has been a need for a large, definitive, high-quality RCT. This study investigated the impact of a short course of oral steroids on inpatients with less severe CAP.

STUDY SUMMARY

Prednisone hastens clinical stabilization, cuts length of hospital stay

In a multicenter, double-blind RCT, Blum et al[1] enrolled 785 patients with CAP admitted to 7 tertiary care hospitals in Switzerland from 2009 to 2014. Patients were eligible for the study if they were ≥18 years old, had a new infiltrate on chest x-ray, and had at least one additional sign or symptom of respiratory illness (eg, cough, dyspnea, fever, abnormal breathing signs or rales, or elevated or decreased white blood cell count). Patients were excluded if they had one of several possible contraindications to corticosteroids, cystic fibrosis, or active tuberculosis.

Patients were randomized to receive either prednisone 50 mg/d or placebo for 7 days. They were treated with antibiotics according to accepted local guidelines; most patients received either amoxicillin/clavulanic acid or ceftriaxone. Antibiotic treatment was adjusted according to susceptibility whenever a specific pathogen was identified. Nurses assessed all patients every 12 hours during hospitalization, and laboratory tests were obtained on hospital Days 1, 3, 5, and 7, and before discharge. Follow-up telephone interviews were conducted on Day 30.

The primary outcome was length of time to clinical stability, which was defined as at least 24 hours of stable vital signs. Stable vital signs was a composite endpoint that required all of the following: temperature ≤37.8°C (≤100°F), heart rate ≤100 beats/min, spontaneous respiratory rate ≤24 breaths/min, systolic blood pressure ≥90 mm Hg (≥100 mm Hg for patients diagnosed with hypertension) without vasopressor support, mental status back to baseline, ability to take food by mouth, and adequate oxygenation on room air.

Secondary outcomes included length of hospital stay, pneumonia recurrence, hospital readmission, intensive care unit (ICU) admission, all-cause mortality, and duration of antibiotic treatment. Researchers also explored whether the rates of complications from pneumonia or corticosteroid use differed between the prednisone and placebo groups.

In an intention-to-treat analysis, the median time to clinical stability was shorter for the prednisone group at 3 days (interquartile range [IQR]=2.5-3.4) compared to the placebo group at 4.4 days (IQR=4-5; hazard ratio [HR]=1.33; 95% confidence interval [CI], 1.15-1.50; *P*<.0001). Median time to hospital discharge was also shorter for the prednisone group (6 days vs 7 days; HR=1.19; 95% CI, 1.04-1.38; *P*=.012) as was duration of IV antibiotic treatment (4 days vs 5 days, difference=-0.89 days; 95% CI, -1.57 to -0.20; *P*=.011).

There were no statistically significant differences in pneumonia recurrence, hospital readmission, ICU admission, or all-cause mortality. Patients treated with prednisone were more likely to experience hyperglycemia that required insulin treatment during admission (19% vs 11%; odds ratio=1.96; 95% CI, 1.31-2.93; *P*=.001).

WHAT'S NEW

This large, good-quality study reinforces previous evidence

This is the largest good-quality RCT to explore the impact of corticosteroid treatment on less severe CAP. Previous studies suggested that corticosteroids may decrease the duration of illness, but this is the first rigorous study to show a clear decrease in both time to clinical stability and length of hospital stay.

Also, this study used an easy-to-administer dose of oral steroids, instead of the several-day course of IV steroids used in most other studies. The findings from this study were incorporated into a 2015 meta-analysis that confirmed that corticosteroid treatment in patients with less severe CAP results in a shorter length of hospital stay and decreased time to clinical stability.[7]

CAVEATS

It's unclear whether steroids can benefit nonhospitalized patients

Because this study included hospitalized patients only, it's not clear whether corticosteroids have a role in outpatient treatment of CAP. Additionally, while this was a large, well-performed study, it did not have a sufficient number of patients to examine whether corticosteroids impact mortality among patients with CAP. Finally, the average length of hos-

The median time to clinical stability was shorter for the prednisone group (3 days) than for the placebo group (4.4 days).

pital stay reported in this study was approximately 1.5 days longer than the typical length of stay in the United States.[2] The average length of stay has varied widely in studies examining corticosteroids in CAP, but good-quality studies have consistently shown a median reduction in length of stay of one day.[7]

CHALLENGES TO IMPLEMENTATION

Steroids carry a risk of adverse events, including hyperglycemia

Treatment with prednisone increases the risk of corticosteroid-related adverse events, primarily hyperglycemia and the need for insulin. This may not be well received by patients or providers. However, these adverse effects appear to resolve quickly after treatment, and do not impact the overall time to clinical stability. JFP

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A supplement to The Journal of Family Practice

Major Depressive Disorder in the Primary Care Setting

STRATEGIES TO ACHIEVE REMISSION AND RECOVERY

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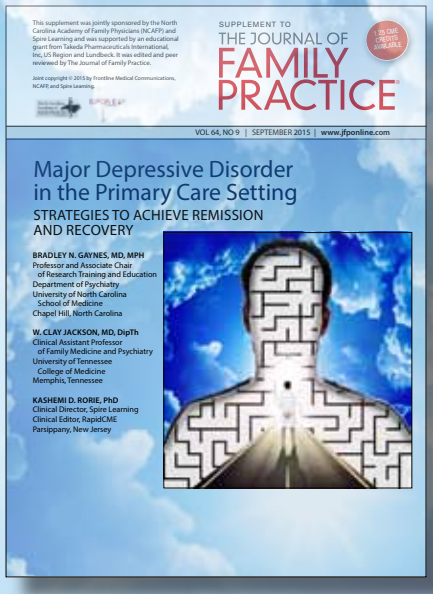

Discussion includes:

- Diagnosis of depression in the primary care setting
- Treatment of depression
- Measurement-based care for major depressive disorder

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