

This Adjunct Medication Can Speed CAP Recovery

Prednisone can help patients with community-acquired pneumonia stabilize more quickly and leave the hospital sooner.

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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 (RCT) and meta-analysis.¹

ILLUSTRATIVE CASE

A 75-year-old woman with hypertension and diabetes presents to the emergency department with shortness of breath, cough, and fever that she's had for four days. On examination, her temperature is 38.2°C; heart rate, 110 beats/min; respiratory rate, 28 breaths/min; and O₂ saturation, 91%. Rhonchi are heard in her right lower lung field; chest x-ray reveals infiltrate in her right lower lobe. The patient is admitted and started on IV antibiotics, IV fluids, acetaminophen for fever, and oxygen. Can anything else be done to speed her recovery?

Community-acquired pneumonia (CAP) is responsible

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for more than 1 million hospitalizations annually in the United States and is the eighth leading cause of death.^{2,3} Treatment of CAP typically consists of antibiotics and supportive measures (eg, IV fluids and antipyretics). Because the disease process 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 six small RCTs that evaluated the impact of corticosteroids on CAP recovery.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 for bias.

Subsequently, a 2012 meta-analysis of nine 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 eight 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 hospital stay

In a multicenter, double-blind RCT, Blum et al¹ enrolled 785 patients with CAP who were admitted to one of seven tertiary care hospitals in Switzerland from 2009 to 2014. Patients were eligible if they were 18 or older, 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 a contraindication to corticosteroids, cystic fibrosis, or active tuberculosis.

Patients were randomized to receive either prednisone 50 mg/d or placebo for seven 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 (eg, at least 24 hours of stable vital signs). This composite endpoint required all of the following: temperature $\leq 37.8^{\circ}\text{C}$; 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 to 3.4) compared to the placebo group at 4.4 days (IQR, 4 - 5; hazard ratio [HR], 1.33). Median time to hospital discharge was also shorter for the prednisone group (6 d vs 7 d; HR, 1.19), as was duration of IV antibiotic treatment (4 d vs 5 d; difference, -0.89 d).

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).

WHAT'S NEW

This large, good-quality study reinforces previous evidence

This is the first rigorous study to show a clear decrease in both time to clinical stability and length of hospital stay. It also 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 if steroids 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, although this was a large, well-designed 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 hospital stay reported in this study was approximately 1.5 days longer than the typical length of stay in the US.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

Risk for adverse events

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

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