Steroids for Community-Acquired Pneumonia: Just Say Yes (Sometimes)

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2019 ATS/IDSA Guidelines on Diagnosis and Treatment of CAP

- Non-severe CAP (strong, high quality of evidence)
- Severe CAP (conditional, moderate quality of evidence)
- Influenza pneumonia (conditional, low quality of evidence)
- CAP + refractory septic shock

The Impact of Pneumonia

- 450 million people affected/year
- #2 diagnosis for hospitalization in U.S.
- 30-day mortality for CAP requiring hospitalization 12%

AHRQ HCUP, 2017
Steroids Improve Survival in Several Infections

- Pneumococcal meningitis
- Tuberculous meningitis
- Tuberculous pericarditis
- Tetanus
- Pneumocystis pneumonia
- Severe typhoid fever


Why Might Steroids Be Useful in Pneumonia?

- Anti-inflammatory effects
- Treatment of critical-illness related corticosteroid insufficiency
- Treatment of non-infectious pneumonia

Multicenter RCT: the Spaniards

120 patients from 2004-2012:
- ≥18 years old
- Clinical symptoms of CAP
- New radiographic opacity
- Met criteria for severe CAP
- CRP >150 mg/L

Methylprednisolone 0.5 mg/kg q12h x 5 days or placebo

Exclusion criteria
- Prior systemic corticosteroids
- Nosocomial pneumonia
- Known immunosuppression
- Life expectancy < 3 months
- Uncontrolled diabetes
- Major GI bleed within 3 months
- Needing > 1 mg/kg/d methylprednisolone
- H1N1 influenza pneumonia

Primary Outcome: Rate of Treatment Failure

**EARLY**
- Within 72 hours
  - Shock
  - Invasive mechanical ventilation
  - Death

**LATE**
- 72-120 hours after treatment
  - Radiographic progression
  - Persistent severe respiratory failure
  - Shock
  - Invasive mechanical ventilation
  - Death

Steroids Reduced Late Treatment Failure

Treatment failure was significantly lower in the steroid group (13%) compared to placebo (31%). No difference in hospital mortality or adverse events

NNT 6

Multicenter RCT: the Swiss

800 patients from 2009-2014
- ≥18 years old
- Radiographic opacity and at least one symptom

Prednisone 50 mg daily for 7 days or placebo

Exclusion criteria
- Active intravenous drug use
- Burns
- GI bleeding within 3 months
- Known adrenal insufficiency
- Condition requiring >0.5 mg/kg/day prednisone
- Pregnancy/breastfeeding
- Immunosuppression

Primary and Secondary Outcomes

**Primary outcome**
- Time to clinical stability

**Secondary outcomes**
- Time to hospital discharge
- Recurrence of pneumonia
- Hospital readmission
- ICU admission
- Mortality
- Duration of antibiotics
- CAP-disease activity scores
- Pneumonia complications
- Corticosteroid side effects


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Steroids Shortened Time to Clinical Stability

- Shorter median time to stability (3.0 days vs. 4.4 days)
- Shorter time to hospital discharge (6.0 vs. 7.0 days)
- Less days of IV antibiotics (4.0 vs. 5.0 days)
- Higher incidence of hyperglycemia requiring insulin in steroid group (19% vs. 11%)


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Let the Meta-analyses Begin…

- 9 randomized controlled trials + 6 cohort studies = 5800 patients
- Mean steroid dose: methylprednisolone 30 mg/day x 7 days


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Cochrane Review

- 17 randomized controlled trials = 2264 patients
- Median steroid dose: prednisone 40-50 mg/day for 5-10 days


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Mortality Decrease From 13% to 8%

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Number Needed to Treat (NNT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT scan for lung cancer screening</td>
<td>217</td>
</tr>
<tr>
<td>Blood pressure medicine for 5 years to prevent death, heart attacks, and strokes</td>
<td>125</td>
</tr>
<tr>
<td>Mediterranean diet for 5 years for heart disease prevention</td>
<td>61</td>
</tr>
<tr>
<td>CABG for preventing death over 10 years</td>
<td>25</td>
</tr>
<tr>
<td>Steroids for severe CAP</td>
<td>18</td>
</tr>
</tbody>
</table>

6 RCTs with 1500 patients: no difference in overall mortality

Intervention | Steroid | Placebo |
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Length of hospital stay, days</td>
<td>7.0</td>
<td>8.0</td>
</tr>
<tr>
<td>Time to clinical stability, days</td>
<td>3.0</td>
<td>4.0</td>
</tr>
<tr>
<td>IV antibiotic treatment, days</td>
<td>4.0</td>
<td>5.0</td>
</tr>
<tr>
<td>CAP-related rehospitalization, %</td>
<td>5.0</td>
<td>2.7</td>
</tr>
<tr>
<td>Hyperglycemia requiring insulin, %</td>
<td>22.1</td>
<td>12.0</td>
</tr>
</tbody>
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What Did the IDSA Find?

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Are Steroids Ever Harmful?

Meta-analysis of 10 observational studies assessing corticosteroids in the treatment of presumed H1N1 influenza-associated complications

Odds ratio 2.12 (95% CI 1.36 – 3.29)

Mean/median dose:
- 67.5 - 117.5 mg/day prednisolone (4 studies)
- 1 - 6 mg/kg/day methylprednisolone (3 studies)


Back to the 2019 ATS/IDSA Guidelines

Some, but not all meta-analyses...have shown a mortality benefit in patients with severe CAP, although no consistent definition of disease severity was used. Side effects of corticosteroids (on the order of 240 mg of hydrocortisone per day) include significant increases in hyperglycemia requiring therapy and possible higher secondary infection rates. No reported study has shown excess mortality in the corticosteroid-treated group.


Pneumonia is a leading cause of hospitalization, mortality, and healthcare costs

Corticosteroids have a plausible mechanism in the treatment of severe CAP

At best, steroids save lives in pneumonia; at worst, they decrease hospital/ICU LOS, time to stability, time on IV antibiotics, and ARDS

Steroids are associated with hyperglycemia, but this can be managed with insulin and the benefits outweigh this risk

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