Pneumonia in the Hospitalized Patient: Use of Steroids

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Facts About Pneumonia

• CAP is the 8th most common cause of death in the USA
• In 2006, 1.3 million hospitalizations for pneumonia.
• 30 day mortality rate for CAP patients requiring hospitalization is about 12%.
Definition of Infectious Pneumonia

- Acute infectious process involving the parenchyma of the lung.
- Requires x-ray evidence or CT chest evidence to really call it pneumonia.
- Pathogens gain access to the lung by micro aspiration, hematogenous spread, direct spread from contiguous focus.
- Despite current diagnostic tests, no pathogen was detected in the majority of patients diagnosed with pneumonia. (23% viral, 11% bacterial, 1% fungal)
Community Acquired LUL Pneumonia
Causes of Radiographic Pneumonia

- Viral infections
- Bacterial infections
- Fungal infections
- Drugs reactions
  - Amiodarone, methotrexate, cancer immunotherapies
- Inhalational exposures
  - Crack cocaine
- Inflammatory causes
  - Systemic vasculitis, BOOP, eosinophilic pneumonia, sarcoidosis
- Pulmonary edema
- Pulmonary embolism with infarct
Community Acquired Bilateral Pneumonia
IDS Guidelines for Treatment of Inpatient Pneumonia

• General Floor Admission
  • Macrolide plus Ceftriaxone
  • Doxycycline plus Ceftriaxone
  • Fluoroquinolone

• ICU Admission
  • Macrolide plus Ceftriaxone
  • Fluoroquinolone plus Ceftriaxone
  • Underlying risk factors: add Vancomycin, add extended spectrum beta lactam
Community Acquired RUL Pneumonia
? Admit or Not ? General Medicine vs ICU

• CURB-65
  • Confusion, Bun >20, RR > 30, BP systolic < 90 or diastolic < 60, Age > 65 yr

• Pneumonia Severity Index (PSI)
  • 20 different risk factors with point assignment and risk stratification I-V

• IDS Guidelines Recommend ICU admission
  • RR>30, PaO2/FiO2 <250, multilobar infiltrate, confusion, BUN>20, WBC<4, platelets<100, T<36, hypotension requiring fluid resuscitation
What is Happening at a Cellular Level in Pneumonia?

• Pathogen enters lungs and innate immune system fails to clear pathogen.
• Cytokine mediated systemic inflammatory response good and bad
  • Local inflammation impairs alveolar gas exchange
  • Systemic inflammation leads to other organ dysfunction
• Dysregulated immune response
• Antibiotics target the invading organism but not the immune system.

• Can systemic steroids attenuate inflammatory response and improve outcome?
CT Chest: RUL pneumonia
Is There a Role for Steroids in Conjunction with Antibiotics?

• Multiple studies have been done suggesting steroids may be beneficial.
  
  • Annals of Internal Medicine 2015
  • JAMA 2015
  • Chest Medicine 2016
  • JAMA 2017
  • Cochrane Database 2017.
Corticosteroid Therapy for Patients Hospitalized with Community Acquired Pneumonia.

- Systematic Review and Meta-analysis: 13 randomized controlled trials for total 2005 patients.
- Examine effect of adjunctive corticosteroid therapy on mortality, morbidity, and duration of hospitalization in CAP.
- Various formulations of steroids used: 1 dose - 10 days.
- All cause mortality 7.9% control group and 5.3% steroid group RR, 0.67 (CI 0.45-1.01)
  - Stratified to severe pneumonia 6 studies RR, 0.39 (CI 0.2-0.77)
- 5% Reduction in need for mechanical ventilation RR 0.45 (CI 0.26-0.79)
- 5% Reduction in risk for ARDS with steroids RR, 0.24 (CI 0.1-0.56)
- Reduction in length of hospitalization by 1 day (CI -1.79 to -0.21)

Annals of Internal Medicine 2015
Effect of Corticosteroids on Treatment Failure Among Hospitalized patients with Severe CAP and High Inflammatory Response.

- Randomized Clinical Trial, double blind, placebo controlled, multicenter
- Severe CAP and CRP > 150mg/L (convert to mmol/L multiply by 9.524)
- Methylprednisolone 0.5mg/kg q12 hr x 5 days vs placebo started within 36 hrs of hospitalization
- Primary outcome: treatment failure (composite outcome early and late)
  - Early treatment failure
    - Development of shock
    - Need for mechanical ventilation
    - Death within 72 hrs
  - Late treatment failure
    - Radiographic progression
    - Persistence of severe respiratory failure
    - Development of shock
    - Need for mechanical ventilation
    - Death between 72-120 hrs

JAMA 2015
Effect of Corticosteroids on Treatment Failure Among Hospitalized Patients with Severe CAP and High Inflammatory Response.

- Secondary outcome:
  - in hospital mortality

- Less treatment failure in steroid group 13% vs 31% (P=.02)
  - Decrease in radiographic progression and late appearance of septic shock

- In hospital mortality rate same
Adjunct Prednisone Therapy for Patients with CAP: a Multicenter, Double-blind, Randomized, Placebo-Controlled Trial

- Prednisone 50mg day vs placebo for 7 days
- Primary endpoint was time to clinical stability
  - Stable vitals for 24hrs, normal mental status, normal oral intake, sats>90% RA
- Total of 785 patients studied
- Median time to clinical stability was shorter in prednisone group 3 days vs 4.4 days (CI 1.15-1.50, p<0.0001)
- No difference in pneumonia associated complications
- Higher incidence of in-hospital hyperglycemia needing insulin 19% vs 11%, CI 1.31-2.93, p=0.001

Lancet 2015
Efficacy and Safety of Corticosteroids for Community-Acquired Pneumonia: A Systematic Review and Meta-Analysis

- 9 RCTs and 6 cohort studies including total of
- Mean steroid use 30mg day methylprednisolone 7 days
- Steroids did not have a statistically significant effect on mortality in CAP (RR, 0.72, CI 0.43-1.21)
- Steroids did not reduce mortality in patients with severe CAP
- Secondary outcomes
  - Steroids were associated with decrease risk of ARDS (RR 0.21, CI 0.08-0.59)
  - Steroids may help reduce LOS in hospital and ICU and time to clinical stability
- Steroids not associated with increased rates of adverse events
Effect of Oral Prednisone on Symptom Duration and Severity in Non-asthmatic Adults With Acute Lower respiratory Track Infection. A Randomized Clinic Trial.

- Assess oral steroids for acute lower respiratory track infections
- 40mg day for 5 days vs placebo
- 398 adults
- Primary outcomes were duration of cough or worse cough and severity of symptoms on days 2 and 4
- No difference in outcomes seen
Steroids in Management of Pneumonia

- Cochrane data base 2017: 17 RCTs for total of 2264 participants, 13 RCTs were adults and 4 RCTs children.
- Trials limited to inpatients with CAP
- Corticosteroids significantly reduced mortality in adults with severe pneumonia (RR 0.58, 95% CI 0.4-0.84)
- Corticosteroids did not significantly reduce mortality in adults with non-severe pneumonia
- Steroids shortened hospital length of stay by about 3 days
- NNT was 18 to prevent 1 death
- Adverse events included hyperglycemia
Recommendations from Uptodate

- Use steroids in patients with CAP who have significant inflammatory response with sepsis and respiratory failure
- Methylprednisolone 0.5mg/kg q 12 hrs or prednisone 50mg day x 5 days
Why Do Steroids Help in Severe CAP?

- Contain an over active immune system that is destroying lung parenchyma
- Steroids are anti inflammatory and are down regulating pro inflammatory cytokines such as IL-6 and IL-8.
- Steroids help to upregulate anti-inflammatory cytokines such as IL-10.
- Relative adrenal insufficiency is treated
- Maybe this is not infectious but mimicking infectious pneumonia
Things to Consider that are Steroid Responsive

- Eosinophilic Pneumonia
- Cryptogenic organizing pneumonia
- Hypersensitivity Pneumonia
- Pulmonary Vasculitis
-ILD
Ct Chest: Diffuse bilateral infiltrates
• 63 yr old female with no significant past medical history presents with 2 day hx of cough, fevers, and dyspnea. She feels tired and looks sick. Temp 102, RR 25, BP 100/70, WBC 3.5, BUN 30, ABG shows pAO2 60, sats 89% and CXR shows dense infiltrate in RLL and RML. Which of the following are correct in regards to best management of this patient?

A. Patient should be treated for pneumonia as an outpatient.

B. Patient may benefit from treatment with methylprednisolone 0.5mg/kg q 12.

C. Patient should be treated with fluoroquinolone plus vancomycin

D. The most common pathogen identified on admission to hospital is streptococcus pneumoniae.
Community Acquired RLL Pneumonia
Question #1

• **Correct Answer:**
  • B) based on current available data, steroids may be beneficial in the management of severe in-patient pneumonia.

• **Explanation:** Cochrane Data base 2017: Corticosteroids significantly reduced mortality in adults with severe pneumonia (RR 0.58, 95% CI 0.4-0.84). Reductions in mortality were not seen in non severe pneumonia.

• Per the IDS guidelines the patient has a score of 3 and should be admitted to the ICU
  • RR>30, PaO2/FiO2 <250, multilobar infiltrate, confusion, BUN>20, WBC<4, platelets<100, T<36, hypotension requiring fluid resuscitation

• Per IDS and ATS guidelines for antibiotics for CAP admitted to the ICU
  • Macrolide plus Ceftriaxone
  • Fluoroquinolone plus Ceftriaxone
  • Underlying risk factors: add Vancomycin, add extended spectrum beta lactam

• Most common pathogens identified on admission to a hospital are viruses but for the majority of cases no pathogen is identified.

Take Home Pearls

• Consider the use of steroids in patients admitted with severe CAP but as a general recommendation this should not be used in all patients admitted with community acquired pneumonia.

• Follow ID guidelines for antibiotics use so we are good stewards of antimicrobial use.

• Vaccinate everyone with flu vaccines and pneumococcal vaccine per guidelines as this intervention will be impactful on this potentially lethal disease.

• Expand your differential diagnosis to noninfectious causes of radiographic pneumonia.

• Better randomized controlled trials are needed to truly answer the question “Should steroids be used in the setting of CAP?”.
References


References


Pneumonia Severity Index

Risk class
Classes 1 and 2 - outpatient management
Class 3 - observation unit or short inpatient stay
Classes 4 and 5 - inpatient management

Pneumonia Severity Index Step 2: Risk factors and assigned points

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic factors</td>
<td></td>
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<tr>
<td>Age for a man</td>
<td>+10</td>
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<tr>
<td>Age for a woman</td>
<td>Age (in years) - 10</td>
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<tr>
<td>Nursing home resident</td>
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<tr>
<td>Coexisting illnesses</td>
<td></td>
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<tr>
<td>Neoplastic disease (active)</td>
<td>+10</td>
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<tr>
<td>Chronic liver disease</td>
<td>+10</td>
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<tr>
<td>Heart failure</td>
<td>+10</td>
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<tr>
<td>Cerebrovascular disease</td>
<td>+10</td>
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<tr>
<td>Chronic renal disease</td>
<td>+10</td>
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<tr>
<td>Physical examination findings</td>
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<tr>
<td>Altered mental status</td>
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<tr>
<td>Respiratory rate ≥30/minute</td>
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<tr>
<td>Systolic blood pressure &lt;90 mmHg</td>
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<tr>
<td>Temperature &lt;35°C or ≥40°C</td>
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<tr>
<td>Pulse ≥125 beats/minute</td>
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<td>Laboratory and radiographic findings</td>
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<td>Arterial pH &lt;7.35</td>
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<td>Blood urea nitrogen ≥20 mg/dL (11 mmol/L)</td>
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<td>Sodium &lt;130 mmol/L</td>
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<td>Glucose ≥250 mg/dL (14 mmol/L)</td>
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<tr>
<td>Hematocrit &lt;30 percent</td>
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<tr>
<td>Partial pressure of arterial oxygen &lt;60 mmHg&quot;</td>
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<tr>
<td>Pleural effusion on chest x-ray</td>
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