IMPLEMENTATION AND ASSESSMENT OF A GUIDELINE-BASED TREATMENT ALGORITHM FOR COMMUNITY-ACQUIRED PNEUMONIA (CAP)

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None of the investigators have conflicts of interest to disclose

IRB status: Approved

Study sponsorship: None
Objectives

- Identify the preferred empiric treatment regimen for patients requiring admission to the hospital for CAP

- Identify one target area to improve antimicrobial therapy for patients with CAP
Background

- Guidelines have increased prescribing homogeneity for empiric antibiotics, but deviations still exist

- IDSA/ATS Guideline recommendation for inpatients (2007)

  - General Inpatient
    - *Beta-lactam + macrolide OR FQ alone*

  - Intensive Care Unit Inpatient
    - *MINIMUM of Beta-lactam + macrolide OR FQ*
    - *Consider MRSA, Pseudomonas? – Specific risk factors*
    - *Local incidence is low*
Background

FDA Drug Safety Communication: FDA advises restricting fluoroquinolone antibiotic use for certain uncomplicated infections; warns about disabling side effects that can occur together

The FDA has issued new information about this safety issue, see the FDA Drug Safety Communication issued July 26, 2016

Safety Announcement

[05-12-2016] The U.S. Food and Drug Administration is advising that the serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh the benefits for patients with acute sinusitis, acute bronchitis, and uncomplicated urinary tract infections who have other treatment options. For patients with these conditions, fluoroquinolones should be reserved for those who do not have alternative treatment options.
Background

- St. Pat’s Infectious Diseases Team agrees with FDA advisory on FQs?
  - Yes – *but there is more*...

- In addition to safety concerns with FQ antibiotics
  - *Broad-spectrum* – covers *Pseudomonas, other important gram (-) bacteria*
  - *One of few synthetic antibiotics* – *low allergenicity*
  - *Antibiotics of good utility*
  - *Reserve for patients who do NOT have other options!*
Background

- St. Pat’s Infectious Diseases and AMS treatment preferences
  - Ceftriaxone 1-2 g daily AND Azithromycin 500 mg daily OR Doxycycline 100 mg BID

- Levofloxacin for patients WITH TYPE 1 BETA-LACTAM ALLERGY

- Anecdotal evidence for FQ and broad-spectrum empiric coverage for CAP locally
  - St. Patrick Hospital AMS team
Methods

- Retrospective, single-center, observational study
- Pre-intervention data collection
- CAP treatment algorithm and provider education
- Post-intervention data collection
- Data gathered via electronic medical record
Methods

- Inclusion criteria
  - Age $\geq 18$ years
  - Patients admitted to hospital
  - Admit diagnosis of CAP

- Exclusion criteria
  - Age $< 18$ years
  - Suspected aspiration pneumonia
  - Admit diagnosis of healthcare-associated pneumonia
  - Diagnosis of hospital acquired and ventilator-associated pneumonia
Methods

- **Primary outcome**
  - Rate of appropriate empiric antibiotic prescribing for inpatients with CAP – as defined within CAP algorithm

- **Secondary outcomes**
  - Antimicrobial duration of therapy (DOT)
  - Time to antibiotic de-escalation or IV to PO
  - Rate of positive microbiology tests
  - Rate of Clostridium difficile infections
  - Length of hospital stay
  - Readmissions within 30 days of discharge
# Results

Table 1. Demographics and clinical characteristics (n = 114)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, mean (standard deviation)</strong></td>
<td>68 (15)</td>
</tr>
<tr>
<td><strong>Male, n (%)</strong></td>
<td>70 (61)</td>
</tr>
<tr>
<td><strong>Comorbid conditions, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>54 (47)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>35 (31)</td>
</tr>
<tr>
<td>Former smoking</td>
<td>47 (41)</td>
</tr>
<tr>
<td>Immunocompromised</td>
<td>15 (13)</td>
</tr>
<tr>
<td>Neoplastic disease</td>
<td>21 (18)</td>
</tr>
<tr>
<td>Liver disease or EtOH use</td>
<td>16 (14)</td>
</tr>
<tr>
<td>CHF</td>
<td>34 (30)</td>
</tr>
<tr>
<td>CKD Stage 3-5</td>
<td>17 (15)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>25 (22)</td>
</tr>
</tbody>
</table>
Results

Treatment location
- General: 75%
- ICU: 25%

CURB-65 Scores
- Zero: 17 (15%)
- One: 43 (38%)
- Two: 32 (28%)
- Three: 18 (16%)
- Four: 4 (4%)
Results

Listed allergies to Beta-lactams

- Type 1 IgE: 8 (7%)
- Non-IgE and intolerances: 12 (11%)
- No reaction listed: 8 (7%)
## Results

### Empiric Antibiotics

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTX AND Azithro OR Doxy</td>
<td>9</td>
<td>8%</td>
</tr>
<tr>
<td>Levo WITH allergy</td>
<td>8</td>
<td>7%</td>
</tr>
<tr>
<td>Levo WITHOUT allergy Broad MDRO coverage</td>
<td>5</td>
<td>4%</td>
</tr>
<tr>
<td>Monotherapy</td>
<td>4</td>
<td>3%</td>
</tr>
</tbody>
</table>

- Appropriate, n=97 (85%)
- Inappropriate, n=17 (15%)
- Indeterminate, n=4 (3%)
Results

Mean Time to PO (hours)

- **Ceftriaxone (n=72)**: 74.4 hours
- **Azithromycin (n=69)**: 32.7 hours
- **Doxycycline (n=2)**: 55 hours
- **Levofloxacin (n=17)**: 73.8 hours
## Results

<table>
<thead>
<tr>
<th>Table 2. Duration of Therapy</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total, median (IQR)</strong></td>
<td>8 (7 to 10)</td>
</tr>
<tr>
<td><strong>Inpatient, median (IQR)</strong></td>
<td>4 (3-7)</td>
</tr>
<tr>
<td><strong>Azithromycin, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>≤3 days</td>
<td>45 (50)</td>
</tr>
<tr>
<td>≥3 days</td>
<td>45 (50)</td>
</tr>
</tbody>
</table>
Results

Antibiotics at discharge

<table>
<thead>
<tr>
<th>Type</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-lactam</td>
<td>56</td>
<td>49%</td>
</tr>
<tr>
<td>Doxy</td>
<td>6</td>
<td>5%</td>
</tr>
<tr>
<td>Levo WITH allergy</td>
<td>6</td>
<td>5%</td>
</tr>
<tr>
<td>None</td>
<td>27</td>
<td>24%</td>
</tr>
</tbody>
</table>

**Appropriate, n=95 (83%)**

**Inappropriate, n=19**

**5 of 8 discharged on levofloxacin were started on preferred therapy**

Levo WITHOUT allergy

Azithro ≥5 days

11 (10%)
## Results

<table>
<thead>
<tr>
<th>Table 3. Length of Stay and 30 day readmissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of hospital stay, median (IQR)</td>
</tr>
<tr>
<td>30 day readmission, n (%)</td>
</tr>
<tr>
<td><strong>Respiratory cause</strong></td>
</tr>
<tr>
<td><strong>Infection</strong></td>
</tr>
<tr>
<td>Other infectious cause</td>
</tr>
<tr>
<td><strong>Other</strong></td>
</tr>
</tbody>
</table>
Discussion

- Analysis of the pre-intervention period revealed good adherence to guidelines as well as local recommendations.

- 3 Infectious diseases physicians with 1 assisting with the study.
  - Rotation to inpatient service every 3 weeks
  - Barrier to algorithm approval

- Many more hospitalists, ED physicians, and Intensivists.
  - Also rotating schedules
  - Anticipate difficulty in education to all providers
Conclusion

- Overall, empiric CAP prescribing is good

- There is always room for improvement
  - Allergy/reaction clarification – role for pharmacists
  - Duration of therapy – Azithromycin
  - Discharging on Levofloxacin after beginning with preferred regimen

- Limitations
  - Retrospective chart review, dependent upon documentation
  - Lacks external validity – local resistance patterns, etc.
Community-Acquired Pneumonia (CAP) Clinical Pathway

Probable/confirmed CAP and inpatient admission

Obtain blood and sputum cultures; consider *S. Pneumoniae* and/or *Legionella* urine antigen

ICU admission?

Type 1 beta-lactam allergy?*

- No
  - Known *Pseudomonas* colonization or risk factors for *Pseudomonas* infection†
    - No
      - Ceftriaxone 1-2 g IV daily
        - **PLUS** Azithromycin 500 mg IV/PO daily
        - **OR** Doxycycline 100 mg IV/PO BID
    - Yes
      - Levofloxacin 750 mg IV/PO daily

- Yes
  - Known *Pseudomonas* colonization or risk factors for *Pseudomonas* infection†
    - No
      - Ceftriaxone 1-2 g IV daily
        - **PLUS** Azithromycin 500 mg IV/PO daily
        - **OR** Doxycycline 100 mg IV/PO BID
    - Yes
      - Levofoxacin 750 mg IV/PO daily
        - +/- Aztreonam 2 g IV q8h

Patient clinically improving at 48-72 hours?‡

- No
  - Consider ID consult
  - Reassess culture and repeat if needed

- Yes
  - De-escalate therapy per culture results or urine antigens
  - Transition to PO agents if able ‡
  - Decide on expected duration of therapy ‡
* **Type 1 Beta-Lactam allergy:** hives, swelling of tongue, lips, eyes, nasal passages or throat, wheezing or shortness of breath, anaphylaxis, documented arrhythmias, hypotension, or patient unsure of reaction or unknown

For complex allergy cases consider infectious disease consult

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**Duration of Therapy**

- Azithromycin: 500 mg daily x3 days or Z-Pak (1.5 g total dose) unless *Legionella* is known or suspected
- Beta-lactams: 5-14 days

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Duration of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No immunocompromise</td>
<td>5 days</td>
</tr>
<tr>
<td>No structural lung disease</td>
<td></td>
</tr>
<tr>
<td>Moderate immunocompromise</td>
<td>7 days</td>
</tr>
<tr>
<td>Moderate structural lung disease</td>
<td></td>
</tr>
<tr>
<td>Poor initial clinical response</td>
<td>10-14 days</td>
</tr>
<tr>
<td>Severe structural lung disease</td>
<td></td>
</tr>
<tr>
<td>Severe immunocompromise</td>
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</tbody>
</table>

- Levofloxacin: 5 days at 750 mg
- Doxycycline: 7-14 days

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**Risk factors for health-care associated pneumonia:**

- Antimicrobials in past 90 days
- Hospitalization ≥2 days in past 90 days
- Current hospitalization >5 days
- Dialysis patient
- Home infusion
- Wound care
- Immunosuppressive therapy or disease
- LTCF resident

**MDRO and Resistant Gram-negative organisms:**

- There are few resistant gram-negative organisms locally
- Double-coverage of gram-negative organisms is not necessary
- See local antibiogram for local resistance patterns

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**Risk factors for *Pseudomonas* infection**

- Known respiratory colonization of *Pseudomonas*
- History of *Pseudomonas* infection
- Bronchiectasis
- Severe COPD requiring frequent steroids and antibiotics

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**MRSA Coverage Considerations:**

- IVDU, post-influenzae, GPC in clusters on sputum gram stain
- Necrotizing empyema
- Negative MRSA nasal swab correlates to ~99% negative predictive value for MRSA pneumonia
Future Directions

- Education
  - *Algorithm*
  - Azithromycin duration of therapy → 1500 mg total treatment dose, especially given infrequency of Legionella
  - Allergy clarification and documentation
  - *Doxycycline and Levofloxacin bioavailability*

- New IDSA/ATS CAP Guideline update in progress

- Reinforcement of preferred empiric antibiotic prescribing
  - *Data shows good adherence to guidelines*
Contact Information

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References


