Procalcitonin as an Antimicrobial Stewardship Tool: Executing antibiotic Use Reduction (PASTEUR)

Jesse M. Inkster, Lyle J. Powell; Laura C. Lammers; Dr. Jim M. Hutchinson; Dr. Richard L. Bachand

Introduction
Community acquired pneumonia (CAP) - Common health problem that hospitalized patients and may lead to death.
- The initiation and duration of antibiotic therapy in CAP is currently based on clinical signs, microbiological testing and radiological findings.
- Overuse of antibiotics in respiratory tract infections comes from overprescribing in less severe patients and extended antibiotic use in more severe cases (e.g. hospitalization and ICU).

What is procalcitonin (PCT)?
- Released by parenchymal cells in response to bacterial toxins
- Rises 2-4 hours after bacterial invasion
- Half-life 22-26 hours
- Rises significantly in bacterial infections however it does not rise or only rises modestly in viral infections and other inflammatory diseases

PCT guided algorithms in CAP
- Reduce antibiotic exposure by 40-50%
- Does not increase mortality or 30 day adverse outcome measures
- Beneficial in determining when to discontinue antibiotics rather than when to initiate them

Objectives
Primary objectives
- To determine if PCT serum monitoring in combination with clinical pharmacist input reduces the number of IV-hospital antimicrobial therapy days.

Secondary objectives
- To determine if PCT serum monitoring in combination with clinical pharmacist input reduces:
  - IV and oral (PO) antibiotic days
  - Hospitalized days, mortality and 30 day re-hospitalization.

Methods
Inclusion Criteria
- Hospitalized patients treated for suspected CAP
- 18-90 years old
- Chest radiograph suggestive of pneumonia or cannot be ruled out
- Presence of at least one of the following acute respiratory signs or symptoms: cough, sputum production, dyspnea, core body temperature exceeding 38.0°C, and leukocyte count greater than 10 x10^9 or less than 4 x10^9 cells/L.

Exclusion Criteria
- Hospital acquired pneumonia and/or health care associated pneumonia
- Severe immunosuppression
- Patients deemed palliative on admission
- Patients with chronic infection necessitating antibiotics
- Patients with documented active intravenous drug use

Table 1: Study Design

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>NRGH</td>
<td>RJH</td>
<td>NRGH</td>
</tr>
<tr>
<td>RJH</td>
<td>NRGH</td>
<td>RJH</td>
</tr>
</tbody>
</table>

Results
Table 2: Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>NRGH (N=40)</th>
<th>RJH (N=44)</th>
<th>NRGH (N=30)</th>
<th>RJH (N=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male</td>
<td>60%</td>
<td>Male</td>
<td>60%</td>
</tr>
<tr>
<td>Age</td>
<td>≥65</td>
<td>70%</td>
<td>≥65</td>
<td>70%</td>
</tr>
<tr>
<td>PSI</td>
<td>≥30</td>
<td>94%</td>
<td>≥30</td>
<td>94%</td>
</tr>
<tr>
<td>Curb-65</td>
<td>≥2</td>
<td>91%</td>
<td>≥2</td>
<td>91%</td>
</tr>
</tbody>
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Table 3: Death Hospital Re-admission and Mean Length of Stay

<table>
<thead>
<tr>
<th></th>
<th>NRGH (N=40)</th>
<th>RJH (N=44)</th>
<th>NRGH (N=30)</th>
<th>RJH (N=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>4%</td>
<td>2%</td>
<td>7%</td>
<td>17%</td>
</tr>
<tr>
<td>Re-admission</td>
<td>3%</td>
<td>1%</td>
<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td>Length of Stay</td>
<td>10.6± 7.5</td>
<td>9.3± 6.2</td>
<td>12.3± 11.5</td>
<td>5.6± 5.1</td>
</tr>
</tbody>
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Figure 5: Percent of Treatments That Could Have Been Stopped Based on PCT Algorithm

Discussion
NRGH retrospectively had significantly more IV and less PO antibiotic days than RJH retrospectively.
- More patients at RJH received oral antibiotic therapy only (7 vs 3).
- RJH had increased length of stay.
- NRGH patients had a higher severity of pneumonia on admission.
- There may have been more patients with contraindications to oral therapy at NRGH.
- Ten patients at NRGH (71 IV antibiotic days) compared to six at RJH (51 IV antibiotic days) received only IV antibiotic therapy.

Protocoled PCT serum monitoring did not significantly reduce total antibiotic days (NRGH prospective vs. RJH prospective).
- Adherence to PCT algorithm was not mandatory.
  - The PCT algorithm suggested antibiotic stop in 58.5% of patients (5.8± 3.0 mean antibiotic days).
  - 14.6% had antibiotics stopped in accordance with the algorithm (4.5± 1.64 mean antibiotic days) → 25% adherence to algorithm
  - Clinical pharmacist follow-up on day shift Monday-Friday only, no weekends or evenings.
  - Chart notes by clinical pharmacist may not have been read.
- RJH and NRGH already had lean prescribing of antibiotics for CAP.

Decreased Oral Therapy (RJH retrospective vs. RJH prospective)
- It was hypothesized that protocoled PCT would encourage IV-PO switch, however there was significantly less PO antibiotic days prospectively.
- Seven patients retrospectively (48 PO antibiotic days, -1.1 mean PO antibiotic days/patient) compared to zero patients prospectively received only oral antibiotic therapy and are not representative of IV-PO switch.

Limitations
- Small sample size with large variation in outcome measures
- Poor documentation in chart notes retrospectively
- CAP antibiotic use limited to hospital only
- No recording of contraindications to oral therapy

Conclusions
- Serum PCT measurement in addition to clinical pharmacists input:
  - Did not significantly reduce PO, IV and total antibiotic days
  - Had no effect on length of hospital stay, death and 30 day read hospitalization
  - PCT should not be ordered to help guide antibiotic therapy in CAP unless there is intention to follow the algorithm.

References available on request – Jesse.Inkster@viha.ca