Clinical Safety & Effectiveness
Cohort # 9

Appropriate utilization of procalcitonin for infections in hospitalized patients

CENTER FOR PATIENT SAFETY & HEALTH POLICY
UT Health Science Center
Educating for Quality Improvement & Patient Safety
Financial Disclosure

Marcos Restrepo, MD, has no relevant financial relationships with commercial interests to disclose.
What We Are Trying to Accomplish?

✓ To increase the knowledge of the appropriate use of procalcitonin from 50% to 75% in health care providers* ordering procalcitonin at the STVHCS by January 10, 2012

✓ To increase the appropriate use of procalcitonin from 41% to 62% (by 50%) in hospitalized patients with presumed infections at the STVHCS by February 16, 2012

* Health care providers = Faculty, fellows, residents and medical students
The Team

• Division
  – CS&E Participant: Marcos I. Restrepo, MD, MSc
  – Team Member: Kelly Echevarria, PharmD
  – Team Member: Jose Cadena, MD
  – Team Member: Gregory Smith, DDS
  – Team Member: Elena Laserna, MD, PhD
  – Team Member: Anisha Arora, MD
  – Team Member: Elizabeth A. Bowhay, MD
  – Facilitator: Amruta D. Parekh, MD, MPH

• Sponsor Department & Mentors
  – Antonio Anzueto, MD -Division Chief (P/CCM) - VA
  – Jay Peters, MD – Division Chief - UTHSCSA
# Project Milestones

- **Team Created**: Sep - 2011
- **AIM statement created**: Sep - 2011
- **Weekly Team Meetings**: Oct-Dec 2011
- **Background Data, Brainstorm Sessions, Workflow and Fishbone Analyses**: Oct-Nov 2011
- **Intervention Design**: Oct-Dec 2011
- **Intervention #1 Implemented**: Jan 10, 2012
- **Data collection**: Jan 11 – Feb 20, 2012
- **Data Analysis**: Feb 21, 2012
- **CS&E Presentation**: Feb, 24 - 2012
Background

What is procalcitonin (PCT)?

- A precursor to calcitonin, a polypeptide hormone that regulates calcium in the blood, vitamin D, and bone metabolism

Produced by the C-cells of the thyroid gland

- The production of PCT is regulated by the CALC-1 gene
- In healthy individuals, PCT is not released into the bloodstream
  - Expression of the CALC-1 gene is restricted to selective expression in the C-cells of the thyroid
    - Normal level is < 0.1 ng/mL
    - Abnormal levels associated with infection and inflammation

eFigure 1. PCT Algorithm for Antibiotic Stewardship

**Procalcitonin (PCT) algorithm for stewardship of antibiotic therapy in patients with LRTI**

- **< 0.1 µg/l**
  - Bacterial etiology very unlikely
  - NO antibiotics!

- **0.1 - 0.25 µg/l**
  - Bacterial etiology unlikely
  - no antibiotics

- **>0.25 - 0.5 µg/l**
  - Bacterial etiology likely
  - Antibiotics yes

- **>0.5 µg/l**
  - Bacterial etiology Very likely
  - Antibiotics YES!

**Control PCT after 6-24 hours**

- Initial antibiotics can be considered in case of:
  - Respiratory or hemodynamic instability
  - Life-threatening comorbidity
  - Need for ICU admission
  - PCT < 0.1 µg/l: CAP with PSI V or CURB65 ≥3, COPD with GOLD IV
  - PCT < 0.25 µg/l: CAP with PSI IV or CURB 65 >2, COPD with GOLD > III
  - Localised infection (abscess, empyema), L.pneumophilia
  - Compromised host defense (e.g. immuno-suppression other than corticosteroids)
  - Concomitant infection in need of antibiotics

**Consider the course of PCT**

- If antibiotics are initiated:
  - Repeated measurement of PCT on days 3, 5, 7
  - Stop antibiotics using the same cut offs above
  - If initial PCT levels are >5-10 µg/l, then stop when 80-90% decrease of peak PCT
  - If initial PCT remains high, consider treatment failure (e.g. resistant strain, empyema, ARDS)
  - **Outpatients**: duration of antibiotics according to the last PCT result:
    - >0.25-0.5 µg/l: 3 days
    - >0.5 - 1.0 µg/l: 5 days
    - >1.0 µg/l: 7 days

**Abbreviations:** PCT procalcitonin, CAP community-acquired pneumonia, PSI pneumonia severity index, COPD chronic obstructive pulmonary disease, GOLD global initiative for obstructive lung disease.
**Procalcitonin to assist Antibiotic therapy**

- **RCT** – PCT vs. Control for the management of respiratory infections on 1359 subjects

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>PCT n=460 - %</th>
<th>Control n=465 - %</th>
<th>* p&lt;0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abx exposure, mean days</td>
<td>7.2</td>
<td>* 10.7</td>
<td></td>
</tr>
<tr>
<td>Abx prescription</td>
<td>91%</td>
<td>* 99%</td>
<td></td>
</tr>
<tr>
<td>Adverse events from Abx</td>
<td>23%</td>
<td>* 33%</td>
<td></td>
</tr>
<tr>
<td>LOS, mean days</td>
<td>10</td>
<td>9.5</td>
<td></td>
</tr>
</tbody>
</table>

Figure 2. Antibiotic Exposure in Patients Receiving Antibiotic Therapy

All patients (n = 1359)

- Time After Study Inclusion, d
- Patients Receiving Antibiotic Therapy, %

Community-acquired pneumonia (n = 925)

- Time After Study Inclusion, d
- Patients Receiving Antibiotic Therapy, %

Exacerbation of COPD (n = 228)

- Time After Study Inclusion, d
- Patients Receiving Antibiotic Therapy, %

Acute bronchitis (n = 151)

- Time After Study Inclusion, d
- Patients Receiving Antibiotic Therapy, %
Meta-analysis of PCT-guided algorithms vs. routine practice

N=7 RCT Studies - (n=1131 ICU patients)

Table 5. Meta-analysis of aggregate dataa: Procalcitonin-guided algorithms versus routine practice

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of antibiotic treatment for the first episode of infection</td>
<td>5</td>
<td>938</td>
<td>WMD (FEM), 95% CI</td>
<td>-2.14 (-2.48 to -1.80)</td>
</tr>
<tr>
<td>Total duration of antibiotic treatment</td>
<td>3</td>
<td>801</td>
<td>WMD (FEM), 95% CI</td>
<td>-4.19 (-4.98 to -3.39)</td>
</tr>
<tr>
<td>Antibiotic-free days</td>
<td>3</td>
<td>801</td>
<td>WMD (FEM), 95% CI</td>
<td>2.94 (1.92 to 3.96)</td>
</tr>
<tr>
<td>28-day mortality</td>
<td>6</td>
<td>1,010</td>
<td>OR (FEM), 95% CI</td>
<td>0.93 (0.69 to 1.26)</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>4</td>
<td>317</td>
<td>OR (FEM), 95% CI</td>
<td>0.86 (0.52 to 1.44)</td>
</tr>
<tr>
<td>ICU length of stay</td>
<td>6</td>
<td>1,010</td>
<td>WMD (FEM), 95% CI</td>
<td>-0.49 (-1.55 to 0.57)</td>
</tr>
<tr>
<td>Hospital length of stay</td>
<td>3</td>
<td>801</td>
<td>WMD (FEM), 95% CI</td>
<td>-0.13 (-1.10 to 0.84)</td>
</tr>
<tr>
<td>Days free from mechanical ventilation</td>
<td>2</td>
<td>722</td>
<td>WMD (FEM), 95% CI</td>
<td>0.60 (-0.64 to 1.85)</td>
</tr>
<tr>
<td>Superinfection rate</td>
<td>3</td>
<td>790</td>
<td>OR (FEM), 95% CI</td>
<td>1.13 (0.83 to 1.54)</td>
</tr>
<tr>
<td>Persistent/relapsed infection rate</td>
<td>3</td>
<td>801</td>
<td>OR (FEM), 95% CI</td>
<td>0.97 (0.56 to 1.69)</td>
</tr>
</tbody>
</table>

Reduction of Antibiotic Prescription and/or duration of Abx

Procalcitonin Appropriate Indications

• Pneumonia
  – CAP
  – HCAP
  – HAP
  – VAP
  – Aspiration

• Sepsis
  – SIRS
  – Sepsis (SIRS plus documented or suspected infection)
  – Severe sepsis (one organ failure)
  – Septic shock (on vasopressors)

• AECOPD
Procalcitonin Inappropriate Indications

• **Localized infection**
  – Skin and soft tissue (abscess, cellulitis)
  – Empyema
  – Osteomyelitis
  – Meningitis
  – Endocarditis
  – Pancreatitis

• **Immunosuppression disease or therapies**
  – Post-transplantation (bone marrow, solid organ)
  – s/p chemo

• **Other**
  – Trauma/post surgery
  – Invasive fungal infection

• **Diagnosis**
  – No infection
  – Unknown diagnosis

• **Time of testing**
  – 1st PCT test value in the middle of an Abx course (no baseline)
PCT use at the VA

• Introduced as a laboratory test
  – January 2011
    • No restrictions
    • No guidelines

• Pre-test evaluation (April 1, 2011 – June 30, 2011)
  – PCT tests n=477
    • 42% Appropriate use
    • 58% Inappropriate use
      ➢ 96% from two services
        » ICU /Intermediate care (62%) or Ward service (34%)
Inappropriate Procalcitonin Order

- Localized infections: 0.23
- No Infections: 0.14
- Immunosuppression: 0.14
- Antibiotics completed: 0.05
- Long term antibiotics: 0.03
- PCT repeated same day: 0.03
Appropriate Procalcitonin Order

UCL 74.9
CL 42.0
LCL 9.1
Cause and Effect Diagram

Cause and effect diagram for Inappropriate use of Procalcitonin
PCT Use Flowchart

How Will We Know That a Change is an Improvement?

• **Measure of Success**
  – Knowledge regarding PCT use
  – Appropriate order of PCT

• **Method of measurement**
  – Pre- and post-test evaluation
  – Retrospective chart review of documented appropriateness of the PCT order

• **Specific targets for change**
  – Increase knowledge of appropriate use of PCT usage
  – Increase effectiveness of appropriate PCT order
Components of the Knowledge Evaluation

• Numerator
  – Number of correct answers by health care providers related to the appropriate usage of PCT

• Denominator
  – Total number health care providers taking the test regarding the appropriate use of PCT

• Testing topic
  – 4 areas of opportunities to appropriate use and order PCT
Components of the PCT Algorithm Evaluation

• **Numerator**
  – Number of appropriate use of PCT orders according to the indications

• **Denominator**
  – Total number PCT tests performed during the study period

• **Algorithm characteristics for appropriate use**
  – Initial testing
  – Follow-up testing
Knowledge Evaluation Sample Characteristics

• Knowledge evaluation
  – Sample population (n=49)
    • Pulmonary and Critical Care fellows (n=12)
    • Medical students (MS 3-4) and internal medicine residents (PGY 1-3) rotating in internal medicine (n=37)
  – Evaluation date
    • January 10, 2012 & December 9, 2011 (for PCCM division)
  – Evaluation characteristics
    • Pre-test
    • Educational program
    • Post test
Clinical Evaluation Sample Characteristics

• Clinical Cohort
  – Sample population
    • Procalcitonin test performed to hospitalized patients at the STVHCS
  – Evaluation period
    • Pre-intervention period
      – April 1, 2011 to June 30, 2011 (14 weeks)
    • Intervention
      – Education program – January 10, 2012
    • Post-intervention period
      – January 11, 2012 to February 16, 2012 (6 weeks)
QI PCT Intervention Implementation

• Phase I
  – Team literature review
  – Developed appropriate usage characteristics
  – Developed algorithm for PCT use
    • Appropriate approvals
    • Dissemination protocols
  – Educational program
    • Baseline knowledge evaluation (students, residents, fellows, faculty)
    • Pre-test assessment prior to an educational program
    • Post-test assessment after the education program
  – Clinical data
    • Pre-clinical data collection and analysis
    • Post-intervention – Phase I: Educational program
    • Post-intervention clinical data collection and analysis
Procalcitonin (PCT) Utilization Guide

Day 1

Suspected Infection
- Lower Respiratory Tract Infections (e.g., CAP, HCAP, HAP, VAP, AECOPD)
- Severe Sepsis & Septic Shock
- Other: (specify)

Collect Micro Samples
Start Antibiotics

PCT Indicated

PCT level

PCT level ≤ 0.25
- Assess severity of disease
  - Low: Consider Stopping Antibiotics
  - Moderate/High: Continue with Antibiotics

PCT level > 0.25
- Any disease severity: Continue with Antibiotics

Clinical Improvement

PCT levels may or may not assist the clinical decision to guide therapy (consider non-infectious process, resistant pathogens, and complications of primary condition)

Not earlier than 5 days on ABX

Check PCT level

PCT level ≤ 0.25
- Consider Stopping Antibiotics

PCT level > 0.25
- Continue with Antibiotics and check culture results and ensure culture-specific antimicrobial if culture positive
- Consider De-escalating empiric therapy
Knowledge Based Evaluation Results

QI PCT Appropriate use
Pre and Post-Tests Answers
Appropriate PCT utilization

<table>
<thead>
<tr>
<th></th>
<th>Pre-test</th>
<th>Post-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appropriate indication</td>
<td>20%</td>
<td>100%</td>
</tr>
<tr>
<td>Appropriate PCT level</td>
<td>70%</td>
<td>100%</td>
</tr>
<tr>
<td>Appropriate Abx use w/Cx+</td>
<td>60%</td>
<td>80%</td>
</tr>
<tr>
<td>Appropriate Abx use w/Cx-</td>
<td>40%</td>
<td>80%</td>
</tr>
</tbody>
</table>
Overall Pre and Post PCT Assessment

P<.001

Pre-test: 50%
Post-test: 84%
Clinical Data Evaluation Results

QI PCT Appropriate use