Procalcitonin: A Review

Crystal Wright, PharmD
PGY-1 Pharmacy Resident
Avera McKennan Hospital & University Health Center
Sioux Falls, SD
February 10th, 2018

Disclosures

- I have had no financial relationship over the past 12 months with any commercial sponsor with a vested interest in this presentation

Learning Objectives

- Pharmacist
  - Identify non-infectious causes of elevated procalcitonin levels
  - Identify patient populations in which evidence supports the utilization of procalcitonin levels to assist in clinical decision making
- Technician
  - Identify non-infectious causes of elevated procalcitonin levels
  - Describe advantages of de-escalation of antibiotics

Background

Procalcitonin

- Prohormone of calcitonin
  - Elevated serum calcium levels
  - Invasion of bacteria or some fungi
- Production
  - Detectable in serum within 4 hours
  - Serum levels peak in 12-48 hours
  - Rarely occurs in response to pure viral infection

Gilbert 2010

Elevated Procalcitonin Levels

- Bacterial infection
  - Pneumonia
  - Sepsis
- Other infection
  - Candidiasis
  - Aspergillosis
- Physiologic stressors
  - Cardiogenic shock
  - Severe burns
  - Pancreatitis
- Medullary thyroid cancer

Patient population	ProCT level (ng/mL)
Stable MTC	3.6
Newly diagnosed MTC	13.8
Recurrent/ metastatic MTC	241.7

Algeciras-Schimnich 2009

Procalcitonin and Infectious Disease

- Why is procalcitonin potentially useful?
  - Assist with determination of causal pathogen
  - De-escalation of antibiotic regimens
- Antibiotic de-escalation
  - Decrease healthcare costs
  - Decreased parenteral compounding
  - Decrease development of antibiotic resistance

SHEA 2012

Guidelines

- IDSA Antimicrobial Stewardship Guideline:
  - "In adults in ICUs with suspected infection, we suggest the use of serial PCT measurements as an ASP intervention to decrease antibiotic use" (weak recommendation, moderate-quality evidence)

Barlam 2016

Sample Protocol

PCT <0.1 ng/mL	PCT 0.1-0.25 ng/mL	PCT 0.26-0.5 ng/mL	PCT >0.5 ng/mL
• Antibiotic therapy strongly discouraged	• Antibiotic therapy discouraged	• Antibiotic therapy recommended	• Antibiotic therapy strongly recommended

- Clinical considerations
  - Consider antibiotic therapy for high-risk patients
  - Significantly elevated PCT on presentation:
    - Decline >80% of peak: stop recommended
    - Decline >90% of peak: stop strongly recommended
  - Recommend serial PCT levels

Albrich 2012

Experience in Clinical Trials

Lower Respiratory Tract Infections

- ProHOSP trial (2009)

Outcome	ProCT (IQR)	Control (IQR)	Rate difference (95% CI)
Antibiotic exposure	5.7 (1-8)	8.7 (6-11)	-34.8 (-40.3 to -28.3)
Antibiotic adverse event rate	19.8%	28.1%	-8.2 (-12.7 to -3.7)
Length of stay	9.4 (4-12)	9.2 (4-12)	1.8 (-6.9 to 11.0)

Schuetz 2009

Lower Respiratory Tract Infections

- Cochrane Review (2017)

Outcome	ProCT	Control	Difference (95% CI)
28-day Mortality	8.6%	10.0%	OR = 0.83 (0.7 – 0.99)
Antibiotic use	8.0 days	9.4 days	-1.83 days (-2.15 to -1.5)
Antibiotic adverse effects	16.3%	22.1%	OR = 0.68 (0.57 – 0.82)

Schuetz 2017

Critically Ill Patients

- PRORATA trial (2010)

Outcome	ProCT group	Control group	P-value
Days without antibiotics	14.3 (SD = 9.1)	11.6 (SD = 8.2)	<0.0001
28-day mortality	21.2%	20.4%	NS
60-day mortality	30%	26.1%	NS

- SAPS trial (2016)

Outcome	ProCT (IQR)	Control (IQR)	P-value
Antibiotic days	5 (3-9)	7 (4-11)	<0.0001
28-day mortality	20%	25%	0.012
365-day mortality	35%	41%	0.007

Bouadma 2010; De Jong 2016

Experience in Clinical Practice

Lower Respiratory Tract Infections

- Albrich, et al (2012)
  - Assessed clinical outcomes in the "real world" as compared to a clinical trial
  - Primary endpoint:

Outcome	ProCT	Control	Absolute difference (95% CI)
Antibiotic exposure	5.9 days	7.4 days	-1.51 (-2.04 to -0.98)

  - Safety endpoints
    - No significant differences found in multiple safety endpoints
    - Fewer antibiotic-associated adverse events in the ProCT group

Albrich 2012

Critically Ill Patients

- Chu, et al (2017)

Outcome	Risk	95% CI
Days of antibiotic therapy	aRR = 1.17	1.15 – 1.18
C. difficile infection	aOR = 1.42	1.09 – 1.85
Mortality	HR = 1.05	0.93 – 1.19

- Discussion
  - Procedures in this study were not consistent with clinical trials
  - Study occurred in different countries – potential for differences in clinical practice

Chu 2017

Learning Assessments

Pharmacist Learning Assessment

- Which of the following disease states could cause an elevated serum procalcitonin level?
  a) Congestive heart failure
  b) Medullary thyroid cancer
  c) Asthma
  d) Osteoporosis
- In the literature, utilization of serum procalcitonin levels to guide therapy in septic patients has resulted in which of the following outcomes?
  a) Decreased 30-day mortality
  b) Decreased 90-day mortality
  c) Decreased duration of antibiotic therapy
  d) Increased length of hospital stay

Technician Learning Assessment

- Which of the following disease states could cause an elevated serum procalcitonin level?
  a) Congestive heart failure
  b) Medullary thyroid cancer
  c) Asthma
  d) Osteoporosis
- Which of the following benefits are gained from de-escalating antibiotic therapy?
  a) Decreased healthcare costs
  b) Decreased likelihood of antibiotic resistance
  c) Decreased risk of secondary infection for patients
  d) All of the above

References

- Albrich WC, Dusemund F, Bucher B, et al; Effectiveness and safety of procalcitonin-guided antibiotic therapy is lower respiratory tract infections in "real life": an international, multicenter, poststudy survey. Arch Intern Med 2012; 172:715-722.
- Algeciras-Schimnich A, Preissner CM, Theobald JP, Finseth MS & Grebe SK. Procalcitonin: a marker for the diagnosis and follow-up of patients with medullary thyroid carcinoma. Journal of Clinical Endocrinology and Metabolism 2009; 94:861–868
- Barlam TF, Cosgrove SE, Abbo LM, MacDougall C, Schuetz AN, Septimus EJ, et al. Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Disease Society of America and the Society for Healthcare Epidemiology of America. Clin Infec Dis 2016; 62:e51-e77.
- Bouadma L, Luyt CE, Tubach F, Cracco C, Alvarez A, Schwebel C, et al. Use of procalcitonin to reduce patients' exposure to antibiotics in intesive care units (PRORATA trial): a multicenter randomized controlled trial. Lancet 2010; 375:463-474.
- Chu D, Mehta AB, and Walkey AJ. Practice Patterns and Outcomes Associated with Procalcitonin Use in Critically Ill Patients with Sepsis. Clin Infec Dis 2017;64(11)1509-1515.

References

- De Jong E, van Oers JA, Beishuizen A, Vos P, Vermeijden WJ, Haas LE, et al. Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomized, controlled, open-label trial. Lancet Infect Dis 2016; 16:819-827.
- Gilbert DN. Use of Plasma Procalcitonin Levels as an Adjunct to Clinical Microbiology. J Clin Mircobiol 2010; 48:2325-2329.
- Schuetz P, Christ-Crain M, Thomann R, et al. Effect of procalcitonin-based guidelines vs standard guidelines on antibiotic use in lower respiratory tract infections: the ProHOSP randomized controlled trial. JAMA 2009; 302:1059-1066.
- Schuetz P, Wirz Y, Sager R, Christ-Crain M, Stolz D, Tamm M, et al. Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections. Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD007498. DOI: 10.1002/14651858.CD007498.pub3.
- SHEA/IDSA/PIDS. Policy Statement on Antimicrobial Stewardship by the Society for Healthcare Epidemiology, the Infectious Disease Society of America, and the Pediatric Infectious Disease Society. Infect Control Hosp Epidemiol 2012;33(4):322-327