PROCALCITONIN: PRO OR CON-ARTIST

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NO DISCLOSURES!

OBJECTIVES

- Discuss how procalcitonin is regulated
- Define the role procalcitonin plays in patient management
- Pitfalls in utilizing procalcitonin

CASE #1

- 64 yo male with PMHx COPD, HTN presents with dyspnea x 1 day, subjective fever and productive cough.
  - VS HR 100 RR 24 BP 150/84 98% RA
  - PE: Alert, tachycardic, mild expiratory wheezing, no knee mottling
  - CXR without infiltrates
  - WBC 14k BMP NL
  - CURB-65 score – 0
  - Procalcitonin – 0.1
    - 0.5
    - 5

CASE #2

- 56 yo male with mild abdominal pain and loose stool. PMHx DM, Obesity, HTN, completed levaquine 1 month ago for sinusitis
  Denies fevers or vomiting
  - VSS HR 90 RR 18 BP 140/85
  - WBC 10.2 BMP NL
  - CT Abdomen – Mild colonic thickening. No perforation or bowel obstruction. NL appendix
  - Procalcitonin - < 0.25

CASE #3

- 45 yo male presents with HA and neck stiffness. Dx with SAH – Hunt Hess grade 2 / Fisher grade 3. Pt is admitted for monitoring and management.
- Pt receives a clipping procedure and close monitoring.
- Postop day 1 – Fever 39 C - Procalcitonin – 20 – No localized infectious process
  - Antibiotics?
- Postop day 5 – afebrile x 24 hrs. HR 95 RR 18 BP 135/84 38.4 C
  - Procalcitonin – 0.1
  - Procalcitonin - 10
- BP 95/50 - ?

PROCALCITONIN

- 116 amino acids
- Stored in extra-thyroidal tissue
  - Lung
  - Liver
  - bowel
- Released in an all or none fashion to stimulus
- Rises in 2-6 hours
- ½ life is 24 hours
- Reduction approximately 30%/day

PROCALCITONIN

- Stimulus is bacterial and trauma predominantly
  - Elevation with H1N1 and H7N9
  - Minimal elevation with atypical bacteria
- Baseline levels are < 0.25
- Linear elevation with level of stimulus
  - Level correlates with outcome
  - Failure to decline correlates with higher mortality
- Trauma and surgery will elevate procalcitonin
  - Return to baseline 48-72 hours
- Appears to rise with age, CKD, and cirrhosis

HISTORY OF PROCALCITONIN

- Discovered in 1981
- Evaluated in LRTI/COPD/CAP
- Most recently expanding into early sepsis recognition
- Studies have looked at:
  - Initiation of antibiotics
  - Continuation of antibiotics

ACUTE PHASE REACTANTS

- CRP vs ESR vs IL-6 vs Procalcitonin
- CRP
  - Elevated in NON-infectious disease e.a. ITP
  - Obesity, smoking, DM, HTN, depression
- ESR
  - Can be influenced by immunoglobulins, neoplasms, ischemia, trauma
  - ESRD, Anemia, SLE
  - Effected by age and gender
- IL-6
  - Not commercially available
- Procalcitonin
  - Sn 77% Sp 90%

LOWER RESPIRATORY TRACT INFECTION

- **Procalcitonin-Guided Antibiotic Use vs a Standard Approach for Acute Respiratory Tract Infections in Primary Care**
  - **53 primary care physicians**
  - **458 patients – required antibiotics**
  - **Procalcitonin (< 0.25 vs > 0.25) vs Standard approach**
  - **Followup at day 7, 14, 28**
- **Results**
  - **Prescription use decreased 72%**
  - **No difference in morbidity or mortality**

Arch Intern Med. 2008;168(18):2000-2007

COPD EXACERBATION

- 208 consecutive patients admitted for COPD exacerbation
- Procalcitonin guided vs standard antibiotic use
- Results
  - Antibiotic use 40% vs 72%
  - Antibiotic exposure 43% vs 73%
  - No difference in morbidity or mortality during hospitalization and at 6 months
  - Number needed to treat – 3

Chest, Volume 131, Issue 1, January 2007, Pages 1-2

ICU – ANTIBIOTIC USE

- Multicentre, prospective, parallel-group, open-label trial
- Non-surgical ICU with anticipated stay > 3 days
- 307 procalcitonin guided vs 314 standard treatment
- Results
  - mortality at 28 and 60 days
    - Procalcitonin guided was noninferior
  - Antibiotic exposure
    - 11.6 days vs 14.3 days

Lancet 2010;375:463-74

Guidelines for initiating antibiotics according to PCT value.
Except any situation requiring immediate therapy ...

PCT ...			
< 0.25 ng/mL	0.25 - 0.5 ng/mL	0.5 ng/mL < 1ng/mL	>= 1 ng/mL
Antibiotics strongly discouraged	Antibiotics discouraged	Antibiotics encouraged	Antibiotics strongly encouraged

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Guidelines for stopping, continuing or changing antibiotics according to daily measured PCT value.

PCT ...			
< 0.25 ng/mL	Decline more than 80% or 80% of peak (maximum) value or ≥ 0.25 to <0.5 ng/mL	Decline of PCT less than 80% of peak value and PCT ≥ 0.5 ng/mL	Increase of PCT above previous and PCT ≥ 0.5 ng/mL
Stopping antibiotics strongly discouraged	Stopping antibiotics encouraged	Continuing antibiotics encouraged	Changing antibiotics strongly encouraged

LANCET 2010;375:463-74

JURY SAYS?

- Meta-analysis
- 14 randomized controlled trials
- 4221 patients
- PCT-guided management
  - Non-inferior

Evid Based Child Health 2013;8:1297-371

JURY SAYS?

- Retrospective data analysis
- 1312 ICU patients
- Arbitrary use of PCT-algorithm
- Result
  - Substantial reduction in treatment costs (DRG system)

Eur J Med Res 2011;16:543-8

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QUESTION

- 1) Procalcitonin can be elevated with the following stimulus?
  - a) Fungemia
  - b) Surgery
  - c) Influenza
  - d) Cellulitis

QUESTION

2) The following is a true statement about procalcitonin

A) It rises in 2-3 hours of a stimulus

B) The procalcitonin level will will halve every 3 days when the source of infection is controlled

C) Procalcitonin is inversely proportional to the bacterial load

D) Procalcitonin level has prognostic implications in CAP

SEPSIS

- AMS
- HYPOTENSION – SBP < 100
- RR > 22

SEPTIC SHOCK

- Persistent hypotension requiring pressor
- Lactate > 2