Procalcitonin and Early Diagnosis of Sepsis

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Sepsis

• Leading cause of mortality in critically ill patients
• Definitions
  – SIRS
    • WBC >12,000 or >10% bands
    • Tachycardia >90
    • Temperature >38 or <36 degrees
    • Tachypnea RR>20 or PaCO2 <32 mm Hg
  – Sepsis = SIRS + Infection
  – Severe Sepsis = Sepsis + Evidence of Organ Failure
  – Septic shock = Sepsis with Hypotension despite adequate volume resuscitation

SIRS/Sepsis

• Diagnosis is often difficult
• SIRS criteria are relatively nonspecific
• Present in numerous illnesses as well as septic patients
• Delays often lead to rapid progression of multiorgan failure, hemodynamic collapse, and death
• Early diagnosis and appropriate antimicrobial therapy is critical to morbidity/mortality reduction
Sepsis

- Delays in diagnosis and institution of therapy leads to rapid increases mortality
- No reliable test to differentiate onset of sepsis vs. other pathology
- Early recognition should therefore lead to decreases in morbidity, mortality, cost, and improve patient outcome
- Reduction in inappropriate use of antimicrobial therapy

Laboratory Markers

- Ideal marker
  - Highly sensitive and specific
  - Clinical correlation with severity of disease
  - Prognostic value
  - Rapid
Diagnosis

• CRP is relatively nonspecific; elevated in a variety of settings including postoperative surgical patients
• Need to differentiate from other inflammatory states such as severe pancreatitis, adrenal insufficiency, autoimmune disease, cardiogenic shock

Procalcitonin

• AA peptide involved in calcium homeostasis

Assay
Assay

Procalcitonin

- Levels > 2 mcg/L are abnormal
- Levels < 0.5 mcg/L – extremely unlikely to be associated with systemic bacterial infections
- Levels > 10 assoc with MODS, septic shock
- Concentration has been shown to be positively correlated with mortality rate
- Unknown why this marker is elevated in severely infectious states
- Elevations seen in nonbacterial infections as well: chemical pneumonitis, parasitic infections, burns

Hamsters given PCT had increased mortality

Procalcitonin

- Rise begins within 2 hours of insult—faster than CRP
- Peaks 8-24 hours and will remain elevated during duration of inflammatory process
- Hamsters given PCT had increased mortality
Drawbacks

- Immediate postoperative period – mild elevations in PCT which may persist until 48 hours
- Not elevated in fungal or viral infections
- Meta analyses and reviews produce conflicting results—may or may not aid in mortality predictions,

Review of existing literature

- Muller et al. studied 101 critically ill patients in a medical intensive care unit
- APACHE II 22+-/-8
- They evaluated serum concentrations of procalcitonin, CRP, IL-6, and lactate
- SIRS (99% pts), sepsis, severe sepsis, and septic shock were diagnosed according to standard criteria
- Broad range of diagnoses, with pneumonia being the most common


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Literature review

- Immunoassay used for detection
- Assay can be completed within 3 hours
- Results:
  - Calcitonin precursors were significantly elevated only in patients with sepsis, severe sepsis, or septic shock \((p<0.01)\)
  - APACHE II, IL-6, and lactate were not significantly different among groups with and without microbiologically documented infection
  - High serum concentrations associated with poorer prognosis

**Literature Review**

- Another prospective study evaluated
  1. The relationship between PCT and other markers of infection/inflammation
  2. Comparison diagnostic/prognostic significance provided by PCT and CRP
- Excluded patients who had had major abdominal and vascular surgery, immunosuppression, pancreatitis
- Samples at admission, 24h, 48h, 120h


**Literature Review**

- Initial measurements of markers do not predict mortality, but decreased levels after 48 hours were seen only in survivors vs. nonsurvivors
- PCT was seen to correlate with clinical severity
- No correlation with serum calcium levels—i.e., PCT is an independent inflammatory mediator
- Conclusion that PCT is correlated with severity and may help to predict chances of survival
Literature review

• PCT may also be useful in guiding the length of the course of antibiotic therapy
• Most patients with community acquired pneumonia receive 7-14 days of antibiotic therapy
• Christ-Crain et al conducted a randomized trial comparing outcomes of patients who were conventionally treated vs those who were treated with a PCT guided strategy
• They were able to demonstrate a reduction in duration of antibiotic therapy as well as a reduction in antibiotic exposure with similar outcomes in both groups


Literature Review

• PCT may also be useful in prediction of ICU mortality risk

Case study

• 78 year old male who is 7 days s/p CABG presents to the Emergency Department with diaphoresis, tachycardia, hypotension
• Given volume resuscitation (2L NS) which temporarily improved hemodynamics
• Labs drawn: CBC, CMP, PT/INR, PCT, CRP
• EKG and echocardiogram ordered
Case Study

• Results:
  – EKG and echo – no evidence of ischemia, no depression of ejection fraction
  – WBC 9,000; PCT 8.4 mcg/L.
• Given elevated PCT, empiric antibiotics started
• CT ordered – demonstrated abscess in sternal wound extending to aortic root