

Procalcitonin or Anti calcitonin? Higher Levels and Correlation with Site of Infection, Co morbidities and Impact on Mortality

This article was published in the following Scient Open Access Journal:

Clinical Microbiology & Case Reports

Received December 20, 2015; Accepted January 18, 2016; Published January 28, 2016

Aditya Shah*, Brian Wolf, Sarah Sansom, Natasha Shah, Sarah Sarfraz, Ankur Dave and Adam Treitman

Advocate Christ Medical Center, University of Illinois Chicago, USA

Background

Procalcitonin (PCT) is a peptide precursor of the hormone calcitonin, the latter being involved with calcium homeostasis. It is composed of 116 amino acids and is produced by Para follicular cells (C cells) of the thyroid and by the neuroendocrine cells of the lung and the intestine [1,2]. The level of procalcitonin rises in a response to a proinflammatory stimulus, especially of bacterial origin. In this case, it is produced, mainly, by the cells of the lung and the intestine [2]. Measurement of procalcitonin can be used as a marker of severe sepsis caused by bacteria and generally grades well with the degree of sepsis, although levels of procalcitonin in the blood are very low [1]. PCT has the greatest sensitivity (85%) and specificity (91%) for differentiating patients with systemic inflammatory response syndrome (SIRS) from those with sepsis, when compared with IL-2, IL-6, IL-8, CRP and TNF-alpha.

There however is a paucity of evidence to compare and contrast the levels of procalcitonin with organism and organ specific sites of infections. It is also not known how this biomarker correlates with age, race, co morbidities and in immunosuppressed patients.

Most studies focus on the levels of the biomarker in an ICU setting [3,4], which show that procalcitonin driven antibiotic escalation have successfully reduced the number of days of antibiotic use and also reduced length of stay in the ICU, however there remains a lot of controversy in the same, as the control group physicians were allowed to veer off protocol if thought clinically necessary, thereby introducing selection bias and other confounders. Studies done outside the ICU focus mainly on respiratory tract infections [5] and procalcitonin level driven therapy in cases of diagnostic uncertainty and in de-escalation of antibiotics. There have only been a few studies which focus on the levels of the biomarker in other sites, namely the urinary tract and gastrointestinal tract [6,7] with very low sample sizes being a limiting factor in the final result analysis.

Methods

Our study patient pool came out to be a total of 135 patients who had positive blood cultures when admitted to the medical and cardiac intensive care unit. Out of the 135, 60 were eliminated due to repeat blood cultures drawn at different points in their hospital stay. Out of the remaining 75, 27 patients did not have a procalcitonin level drawn when in the intensive care unit. We hence narrowed down our pool to a total of 48 patients. Data was collected from Care Connection EMR at Advocate Christ Medical Center looking at patients with medical and cardiac intensive care unit admissions during the dates listed above with both positive blood cultures and a procalcitonin level drawn within 24hrs of the positive blood cultures being drawn.

Between group comparisons for procalcitonin were assessed using independent samples t-tests and associations were assessed using Pearson's correlations. Analysis was performed using SPSS@22 and statistical significance will be determined at $p \leq 0.05$.

Inclusion criteria

1. Age > 18 years
2. Admission to Advocate Christ Medical Center, inpatient in the Medical and Cardiac ICU

*Corresponding author: Aditya Shah, Advocate Christ Medical Center, University of Illinois Chicago, 4440 W 95th Street, Oak Lawn, IL 60453, USA, Tel: 513-629-2931, Email: Aditya.Shah@advocatehealth.com

3. At least 1 positive blood culture drawn within 24 hours of a PCT level being drawn
4. PCT level drawn within 24 hours of positive blood cultures being drawn

Exclusion criteria

1. Age < 18 years
2. No Procalcitonin level drawn
3. No blood cultures drawn. This was a retrospective study of patients who were admitted to Advocate Christ Medical Center MICCU between December 1 2013-November 30 2014, based on the inclusion and exclusion criterion listed.

Data points collected were as follows:

1. Race
2. Age
3. Blood cultures:
 - A. Organism identified in blood culture
 - B. True or False positive blood cultures as documented by physician notes
 - If false positive blood cultures documented, were verified by chart review by Infectious Disease physicians listed in this IRB
 - False positive blood cultures included coagulase negative staphylococcus and diphtheroids with likely other, non-bacterial source of sepsis
 4. Originating source of bacteremia infection included:
 - A. Lung
 - B. Line infection
 - C. Skin or soft tissue
 - D. Intra abdominal
 - E. Urinary tract
 5. Co morbidities included:
 - A. CHF: 2D ECHO documentation of systolic dysfunction with reduced ejection fraction (left ventricular ejection \leq 40 percent) or diastolic dysfunction (as read on the ECHO, moderate and severe) with left ventricular EF \geq 50 percent
 - B. Acute renal failure: (Increase in serum creatinine by \geq 0.3 mg/dL (\geq 26.5 micromol/L) within 48 hours; or Increase in serum creatinine by \geq 1.5 times baseline, which is known or presumed to have occurred within the prior seven days), CKD (Stage 1 to stage 5 with GFR less than 90) or ESRD (Complete loss of kidney function (eg., need for renal replacement therapy) for more than three months)- Patient on dialysis or presenting with GFR < 15 based on labs drawn during PCT level measured
 6. Systemic inflammatory response syndrome criterion at time of PCT level drawn including:
 1. Temperature
 2. Respiratory rate

3. Heart rate
4. White blood cell count
7. Pregnant- Yes or No

Analysis was done using common statistical parameters.

Results

The main findings of our study were:

Mean PCT levels:

P value 0.067	Mean
Intra abdominal	19.54 \pm 22.14
Lung	3.55 \pm 7.64

	r	P value
Kidney dysfunction	0.541	<0.001

PCT levels were higher in patients with kidney dysfunction, (r=0.541, p<0.001)

	Positive blood cultures	Others
Mortality in ICU	58%	35%

There were no statistically significant differences between mean PCT levels for true versus false positive blood cultures (53.63 \pm 130.52 versus 24.21 \pm 61.34, p=0.61), congestive heart failure, age, and race.

Conclusion

We present a retrospective pilot study investigating PCT levels in ICU patients in relation to multiple variables. Our study shows a trend of higher PCT levels in intra-abdominal compared to lung infections, and elevated PCT levels in patients with kidney dysfunction. Mortality in patients with positive blood cultures was also higher than average ICU mortality at the study center. There was no statistically significant difference found between the other studied variables including true and false positive blood cultures. Due to small sample size, the power was limited.

Limitations of the study were a small sample size, total of 48. There were a few confounding variables, with regards to patient demographic, co-morbidities and acuity of the population. The study was also a single center study with inherent limitations that a retrospective study entails.

Our research group is going to aim to expand the scope of the study, with regards to increasing sample size by increasing the time frame of the IRB. Aim to go into the complexities of the study, by trying to research species-specific procalcitonin levels. Aim to look at procalcitonin levels, before and after the administration of antibiotics and their trend as patient improves.

References

1. Chiesa C, Panero A, Rossi N, et al. Reliability of procalcitonin concentrations for the diagnosis of sepsis in critically ill neonates. *Clin Infect Dis*. 1998;26(3):664-672.
2. Becker KL, Nylén ES, White JC, Müller B, Snider RH Jr. Procalcitonin and the calcitonin gene family of peptides in inflammation, infection and sepsis: a journey from calcitonin back to its precursors. *J Clin Endocrinol Metab*. 2004;89(4):1512-1525.
3. Bouadma L, Luyt CE, Tubach F, et al. Use of procalcitonin to reduce patient's exposure to antibiotics in intensive care units (PRORATA trial): a multi center randomized controlled trial. *Lancet*. 2010;375(9713):463-474.

4. Shehabi Y, Sterba M, Garrett PM, et al. Procalcitonin algorithm in critically ill adults with undifferentiated infection or suspected sepsis. A randomized controlled trial. *Am J Respir Crit Care Med*. 2014;190(10):1102-1110.
5. 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(10):1059-1066.
6. Park JH, Wee JH, Choi SP, Park KN. Serum procalcitonin level for the prediction of severity in women with acute pyelonephritis in the ED: value of procalcitonin in acute pyelonephritis. *Am J Emerg Med*. 2013;31(7):1092-1097.
7. Herrlinger KR, Dittmann R, Weitz G, et al. Serum Procalcitonin Differentiates Inflammatory Bowel Disease and Self- limited Colitis. *Inflamm Bowel Dis*. 2004;10(3):229-233.