The Utility of Procalcitonin in Elderly Patients with COPD Exacerbation

Razi Syed¹, Daniel H. Havlichek²*, Gary E. Stein², Curtis L. Smith³

¹Department of Medicine, Division of Infectious Disease, College of Human Medicine, Michigan State University, East Lansing, 48824, Michigan
²Department of Medicine, College of Human Medicine, Michigan State University, East Lansing, 48824, Michigan
³Department of Pharmacology, Ferris State University, Lansing, 48909, Michigan

*Corresponding Author: Daniel.Havlichek@hc.msu.edu

Copyright © 2014 Horizon Research Publishing All rights reserved.

Abstract  OBJECTIVES: To determine the usefulness of Procalcitonin (PCT) in detecting bacterial infection in hospitalized elderly patients with COPD exacerbation. DESIGN: Prospective observational study to compare PCT levels in patients with and without pneumonia. SETTING: Acute care community hospital in United States. PARTICIPANTS: 18 elderly patients age 65 years and older admitted to an internal medicine ward. MEASUREMENTS: Demographic characteristics, general signs and symptoms, laboratory and chest radiographic results, PCT levels, antibiotic use and duration, length of hospital stay and 90-day readmission rates. RESULTS: Eight (44%) patients had a diagnosis of pneumonia. Procalcitonin levels suggestive of a bacterial infection were found in only four patients and each of these patients had pneumonia. Three patients with pneumonia had positive sputum cultures without an elevated PCT level. No patient without pneumonia had an elevated PCT level. The sensitivity and specificity for predicting a bacterial pneumonia in our patients was 50% (95% CI, 16-84%) and 100% (95% CI, 69-100%), respectively. This biomarker had a positive predictive value of 100% (95% CI, 40-100%) and a negative predictive value of 71% (95% CI, 42-91%) CONCLUSION: Our study results suggest that PCT is not sufficiently sensitive to be used as a diagnostic test of bacterial infection in elderly patients with COPD exacerbation. It may assist clinicians in identifying patients without pneumonia who do not require antibiotics due to its high specificity and negative predictive value.

Keywords  Procalcitonin, COPD, Elderly, Infection

1. Introduction

The use of antibiotics in patients with chronic obstructive pulmonary disease (COPD) exacerbation is controversial and depends upon the severity and nature of reported symptoms [1]. Antibiotics are recommended for moderate to severe exacerbations when there is increased dyspnea, sputum volume, and purulence, but recent evidence suggests that a true bacterial infection represents a complex process that often includes acquisition of a new bacterial strain [2]. Identifying appropriate patients for antibiotic treatment remains a challenge even with positive cultures because sputum cultures do not distinguish between invasive infection and colonization [3].

Procalcitonin (PCT) is an acute inflammatory phase protein that has been studied as a biomarker of bacterial infection for the past 20 years [4]. Its upregulation correlates with severity and extent of bacterial infection. The use of PCT in patients with COPD exacerbation is of interest because PCT levels are not elevated in patients with viral respiratory tract infection or bacterial colonization [5]. Therefore, PCT levels could assist in clinical decisions regarding whether patients with COPD exacerbations would benefit from antibiotic therapy [6].

Several studies have been conducted concerning the interpretation and usefulness of PCT levels in elderly patients [7, 8]. Different outcomes as well as different populations of patients have been studied. In general, PCT performed poorly in diagnosing bacterial infection with the exception of patients with or without bacteremia [9]. A comparative bacterial analysis of elderly patients with COPD exacerbation with or without pneumonia has not been performed. In this preliminary investigation, we studied hospitalized elderly patients with COPD exacerbation. Our objective was to assess PCT as a biomarker of bacterial infection in patients with and without pneumonia.

2. Patients and Methods

Elderly patients (≥65 years) with a past history of COPD who were admitted to the hospital for COPD exacerbation or pneumonia were eligible to enroll into this study. All patients defined as having pneumonia had new infiltrate on chest
radiograph plus either fever, new cough, pleuritic chest pain, worsening dyspnea, or altered breath sounds. The admitting physician diagnosis and management plan were used to categorize patients as COPD exacerbation or COPD with pneumonia. Patients were excluded if they had received antibiotics within 10 days of admission, were immunocompromised, had severe sepsis, or were receiving > 20 mg/d of prednisone. All patients signed a written informed consent that was approved by the hospital investigational review committee prior to study entry.

Patient demographic data, vital signs, laboratory and chest radiographic results, antibiotic use, and length of hospital stay were recorded and analyzed. Readmission rates to the hospital over the next 3 months were also documented. Patients were defined as having clinical pneumonia if they had a new infiltrate on chest radiograph along with fever or increased cough.

Serum for determining PCT levels was obtained from each patient and stored at -70°C. Procalcitonin assays were performed using the mini VIDAS system (bioMerieux; Marcy, France). The reference ranges and interpretations we employed to analyze our results are in Table 1 [10]. The PCT levels were determined at the end of the study and not available to the clinicians caring for these patients.

Statistical analyses were performed using SPSS, version 19 (SPSS, Inc. Chicago, IL). Analysis of continuous variables was performed using the Mann-Whitney U test. The Fishers Exact test was utilized for analysis of categorical variables. A P value of ≤ 0.05 was considered statistically significant.

### Table 1. Procalcitonin Reference Ranges and Interpretations

<table>
<thead>
<tr>
<th>PCT level (ng/mL)</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.1</td>
<td>Bacterial infection highly unlikely</td>
</tr>
<tr>
<td>0.1 to &lt; 0.25</td>
<td>Unlikely bacterial infection</td>
</tr>
<tr>
<td>0.25 to &lt; 0.5</td>
<td>Likely bacterial infection</td>
</tr>
<tr>
<td>≥ 0.5</td>
<td>Bacterial infection highly likely</td>
</tr>
</tbody>
</table>

### 3. Results

A total of 18 patients with COPD exacerbation were enrolled into this study. Eight (44%) of these patients also had a diagnosis of pneumonia. In general, these patients had similar demographic characteristics and vital signs. Patients with pneumonia tended to be older (79 years vs. 74 years, p = 0.03) and had higher mean WBC counts (16,000/mm³ vs. 8,000/mm³, p = 0.03) on admission to the hospital. Antibiotics were initiated in 16 (89%) of the 18 enrolled patients. A respiratory pathogen was isolated from sputum samples in 4 (50%) patients with pneumonia but only 1 (10%) patient without pneumonia (p = 0.11). No patient had positive blood cultures.

Procalcitonin levels suggestive of a bacterial infection (≥ 0.25 ng/mL) were found in only 4 patients. All patients with elevated PCT levels had pneumonia. Only one patient had both an elevated PCT level and a positive sputum culture (Table 2). The sensitivity ± confidence interval (CI) of PCT for predicting a bacterial pneumonia in our patients was 50% (95% CI, 16-84%). The specificity of PCT in our patients was 100% (95% CI, 69-100%) with a positive predictive value of 100% (95% CI, 40-100%) and a negative predictive value of 71% (95% CI, 42-91%).

### Table 2. Procalcitonin Levels in Patients with Positive Sputum Cultures

<table>
<thead>
<tr>
<th>PCT Level (ng/mL)</th>
<th>Nonpneumonic</th>
<th>Pneumonic</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.05</td>
<td>Moraxella catarrhalis</td>
<td>--</td>
</tr>
<tr>
<td>0.06</td>
<td>--</td>
<td>E. coli</td>
</tr>
<tr>
<td>0.07</td>
<td>--</td>
<td>Strep. pneumonia</td>
</tr>
<tr>
<td>0.09</td>
<td>--</td>
<td>Serratia marcescens</td>
</tr>
<tr>
<td>0.47</td>
<td>--</td>
<td>Staph. aureus</td>
</tr>
</tbody>
</table>

Non pneumonic patients had a similar length of hospitalization as those with pneumonia (7d vs. 8d). The duration of antibiotic treatment was also not statistically different in these two groups (5d vs. 7.5d). Hospital readmission rates were the same in patients with and without pneumonia (50% in each group).

### 4. Discussion

Distinguishing the various causes of lower respiratory tract infection (LRTI) can be difficult because their clinical presentations are similar [6]. In patients with COPD, bacterial colonization of sputum is also a confounding factor in determining the need for antibiotic therapy [2]. The judicious use of antibiotics in patients with LRTIs is important to help decrease hospital and patient costs, lower the incidence of adverse events, and address concerns about antibiotic resistance [2].

Recent studies indicate that serum PCT levels can be used to guide antibiotic prescription for patients with LRTIs including patients with COPD exacerbation [5]. Procalcitonin levels are often higher in patients with pneumonia and can independently distinguish these patients from those with COPD exacerbation without pneumonia [11]. The application of a PCT- guided approach to antibiotic therapy is likely to have the greatest effect in the subset of patients with a low-to-intermediate risk of bacterial infection since most nonpneumonia LRTIs are viral in origin [6]. In patients with COPD exacerbation, Stolz et al. found that PCT guidance helped reduce antibiotic use without increases in relapse or decline in lung function [12]. Similar findings were observed by Kristoffersen and colleagues in patients with COPD admitted to the hospital with suspicion of pneumonia [13]. However, Daniels et al. found that patients with acute exacerbations of COPD without pneumonia
exhibited benefit from antibiotics even with a low PCT level [14].

In our subset of patients admitted to the hospital without clinical pneumonia, none had a PCT level ≥ 0.25 ng/mL (likely bacterial infection). Eight (80%) of these patients received antibiotics for a mean duration of 5 days. Knowledge of PCT levels in these patients may have decreased antibiotic use based upon its negative predictive value [9]. In a study of hospitalized adult patients with exacerbation COPD, Bafadhel et al. found that antibiotic use could be reduced from 76% to 7% (reduction of 91%) using a PCT level of > 0.25 ng/mL to guide antibiotic therapy [15]. In our patients with clinical pneumonia, there was a lack of sensitivity (50%) of PCT levels and this biomarker was elevated (> 0.1 ng/mL) in only one case where a pathogen was isolated from sputum (Table 2). This low sensitivity in predicting invasive infection is similar to previous studies of elderly patients [7, 8].

In summary, our study results are in agreement with previous investigations which discovered that PCT is not sufficiently sensitive to be used as a diagnostic test of a bacterial infection in elderly patients with LRTI. Due to its high negative predictive value in patients with COPD exacerbation without definitive pneumonia, it can assist clinicians in identifying patients at initial clinical presentation who do not require antibiotics.

REFERENCES