Utility of streptococcus pneumoniae urinary antigen test for patients with bacteremic pneumococcal community-acquired pneumonia (CAP)

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ABSTRACT

Introduction

The Streptococcus pneumoniae (Sp) urinary antigen test (UAT) is a standard microbiological test in hospitalized patients with CAP. The Sp-UAT detects Sp C polysaccharide, a cell wall component that is present in all Sp serotypes. Patients with CAP with positive blood cultures are considered to have a high Sp antigen load. In these patients, it would be expected that high levels of C polysaccharide would be present in the urine. Therefore, Sp-UAT should be positive in most patients with Sp CAP bacteremia.

Objective

The objective of this study was to define the ability of the Sp-UAT to detect Sp CAP in patients with Sp bacteremia.

METHODS

This was a secondary data analysis of the Community-Acquired Pneumonia Organization (CAPSO) International Cohort Study database. Patients with bacteremic Sp CAP in whom blood cultures and the Sp-UAT were obtained were included in the analysis. The percentage of patients in whom a positive Sp-UAT was documented was calculated.

RESULTS

A total of 86 patients were included in the study. Forty patients (47%) with bacteremic Sp CAP had a positive Sp-UAT.

Conclusions

This study indicates that the Sp-UAT is a poor diagnostic test in patients with bacteremic Sp CAP. This finding may indicate that some patients with bacteremia may not have a high bacterial load and the Sp C polysaccharide may not be present in the urine. Alternatively, all patients with bacteremia may have Sp C polysaccharide in the urine and the sensitivity of the Sp-UAT may not be adequate.

INTRODUCTION

Community acquired pneumonia (CAP) is associated with a high morbidity and mortality worldwide, with estimates of over four million deaths each year and ranks second in United States in terms of health related deaths. Streptococcus pneumoniae (Sp) is the most common etiology of CAP, however, definite and timely microbiological diagnosis is challenging. Blood cultures are considered as a definitive diagnosis for CAP. Studies have shown that blood cultures have high specificity and poor sensitivity, whereas sputum cultures have high sensitivity and low specificity. It has been demonstrated that blood cultures are positive in only 20–25% of pneumococcal pneumonia patients. In terms of sputum cultures, only 50% of the samples are adequate which makes the test results unreliable. Thus, both these tests can’t provide an accurate diagnosis as well as they can be negative as a result of prior antibiotic use. The Sp urinary antigen test (UAT) is a standard microbiological test in hospitalized patients with CAP. It is aimed at analyzing the pneumococcal C polysaccharide excreted in urine and is a fairly new approach for the definitive diagnosis of pneumococcal CAP. This is a simple and rapid technique with results only in 15 minutes, thus it benefits the early institution of directed antibiotic therapy which in turn will decrease the associated mortality and morbidity. Binax NOW® UAT is one of the tests that can be used clinically for the identification of Sp. It is an immunochromatographic assay that uses a rabbit anti-S. pneumoniae antibody, conjugated to visualizing particles, to bind any soluble pneumococcal antigen (C polysaccharide) present in the urine sample. Various studies have studied the efficacy of Sp-UAT in diagnosing bacteremic Sp CAP, highlighting that the test results are positive in 60–85% of patients with definitive Sp CAP and in only 40–65% of those who have presumptive Sp CAP. Patients with CAP with positive blood cultures are considered to have a high Sp antigen load. In these patients, it would be expected that high levels of C polysaccharide would be present in the urine. Therefore, Sp-UAT should be positive in most patients with Sp CAP bacteremia.

Study design and Study population:

This was a secondary analysis of patients enrolled in the Community-Acquired Pneumonia Organization (CAPSO) international cohort study. Data were collected from between 2001 and 2015. In each participating center, non-consecutive medical records of hospitalized patients with the diagnosis of CAP were reviewed. A sample of the data collection form is available at the study website (www.capositie.com). Validation of data quality was performed at the study center before the occurrence in the CAPSO database. Institutional Review Board approval was obtained by each participating center.

Study definitions

CAP: Diagnosis of CAP required the presence of criteria A, B, and C:
A. New pulmonary infiltrate on imaging (CT scan or chest x-ray) at the time of admission to the hospital.
B. Signs and Symptoms of CAP (at least one of the following):
1. Fever >37.8°C (100°F) or hypothermia <35.6°C (96.0°F).
2. Changes in WBC (leukocytosis >11,000 cells/mm²), left shift >10% band forms/microtubes, or leukopenia <4,000 cells/mm².
C. Working diagnosis of CAP at the time of hospital admission with antimicrobial therapy given within 24 hours of admission.

Bacteremic Sp CAP, defined as those patients who had Sp isolated in blood cultures.

Study Groups:

The patients were divided into two groups:
Group A - Sp-UAT positive for Sp
Group B - Sp-UAT negative for Sp

Statistical analysis

Baseline categorical explanatory variables were summarized as frequencies and percentages and differences between both groups of patients were analyzed using a chi-square test or Fisher’s exact test when appropriate and warranted. Continuous variables were summarized as frequencies and interquartile range and differences between groups were analyzed by Wilcoxon-Mann-Whitney test.

The percentage of patients in whom a positive Sp-UAT was documented was calculated.

RESULTS

A total of 86 patients who had blood cultures positive for bacteremic Sp CAP and UAT obtained were evaluated for the study.

Study Flowchart is depicted in Figure 1.

Patient characteristics are shown in Table 1.

Figure 1: Study Flowchart: Correlation of positive blood cultures to Urinary antigen test

CONCLUSIONS

The results of the current study demonstrate that Sp-UAT is a poor diagnostic test for the identification of the causative agent of CAP in bacteremic Sp CAP patients. Molinos et al. analyzed data from 3,874 CAP patients, reporting the sensitivity and specificity of Sp-UAT to be 60% and 97.9% respectively. These results indicate that Sp-UAT is a good test for ruling Sp in but not ruling it out. However, it was noted that the probability of diagnosing bacteremic Sp CAP was affected by the presence of various factors including disease severity (pneumonia severity index), prior antibiotic administration, and decreased renal function. They found the probability to be 12% with presence of one factor and increase in probability to 52% with the presence of six or more factors. This emphasizes that the Sp-UAT is not an adequate diagnostic test as its results vary with various factors which affect the intravascular burden of bacteria. The results of Sp-UAT can also be negative due to dilution of the urine samples. Decrease in the levels of serum Sp C polysaccharide and sequestration of the antigen by binding to the serum antibodies in immune complexes can also affect urinary level of antigen, ultimately affecting the results. These factors can also attribute to the ineffectiveness of the UAT.

Limitations of the study include small sample size which influences the significance of test results. Sensitivity and specificity of the Sp-UAT could not be calculated because of the absence of data of the blood culture negative CAP patients. Further prospective multicenter randomized controlled trials are required to evaluate the efficacy of UAT in identification of Sp-in pneumococcal pneumonia patients.

REFERENCES

