

Assessment of a urinary antigen test in inpatients with pneumococcal pneumonia

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BACKGROUND: Streptococcus pneumoniae is one of the most important pathogens in community-acquired pneumonia. Diagnosis of this disease by conventional methods is often problematic. Therefore, a sensitive and specific diagnostic method can be helpful. The aim of this study was to evaluate the sensitivity and specificity of a rapid urinary antigen detection test in patients with pneumonia. **METHODS:** In a cross-sectional study, a total number of 66 patients including 47 (71.2%) males and 19 (28.8%) females over 18 years old were divided into two groups. The case group included 33 patients with pneumococcal pneumonia while the control group consisted of 33 patients with non-pneumococcal pneumonia. We compared the sensitivity and specificity of an in-vitro rapid immunochromatography (IC) pneumococcal urinary antigen test between the two groups. **RESULTS:** While 23 patients (69.7%) in the case group had positive urine antigen test results, no control patient with positive urine antigen test result was detected. The sensitivity of urinary antigen test in the case group was 69.70% (95% CI: 51.29-84.38). The specificity of the test was determined as 100% (95% CI: 89.32-100). Positive and negative predictive values of the test were 100% (85.05-100) and 76.74% (61.36-88.23), respectively. **CONCLUSIONS:** Pneumococcal urinary antigen IC test is a sensitive and highly specific method for diagnosis of pneumococcal pneumonia.

KEYWORDS: Urine Antigen, Community-Acquired Pneumonia, Pneumococcal Pneumonia, Pneumococci

BACKGROUND

Streptococcus pneumoniae (SP) still remains one of the major pathogens in adults and children worldwide. It is responsible for more than 5,000,000 pneumonia cases every year.^[1] With a significant mortality rate, it is still considered as a killer disease.^[1] SP finds its ecological niche in colonizing the nasopharynx. An appropriate culturing would yield pneumococci in up to 40-60% or greater.^[2] When potentially different protective defenses are suppressed due to various diseases and environmental factors, pneumococci access to alveoli by microaspiration. The organism produces several virulence factors that are involved in the diseases.^[3] SP is the leading cause of community-acquired pneumonia (CAP) and a significant cause of morbidity and mortality in all age groups.^[4] The causative role of SP is strongly suggested by microscopic examination of Gram-stained sputum culture⁵ and approved by blood culture.^[2] Microscopic examination and culture of expectorated sputum remain the mainstay of the laboratory evaluation of pneumonia.^[1,5] Failure to determine CAP etiology results from limitations in these routine diagnostic methods. The diagnosis of pneumococcal pneumonia is frequently problematic. In pre-antibiotic era, only about 25% of patients had positive blood culture.^[6]

However, the rates further decrease when antibiotics had been previously administered.^[7] Difficulties in obtaining good-quality sputum and lag time in receiving conventional culture and unavailability of new culture methods in every hospital are the reasons to seek for new rapid and accurate diagnostic methods. Conventional multiplex polymerase chain reaction (PCR) and novel real time PCR are insufficiently sensitive when applied to blood or urine and are not infection specific when applied to respiratory samples.^[8] Urinary pneumococcal antigen detection is considered as a possible diagnostic utility.^[9] BinaxNOW® (Inverness Medical, Cologne, Germany) is an in-vitro rapid immunochromatographic test (ICT) for the qualitative detection of C polysaccharide SP antigen in urine of patients with pneumococcal pneumonia.^[10,11] The aim of this study was to evaluate the sensitivity and specificity of this urinary antigen detection test in inpatients with diagnosis of pneumococcal pneumonia.

METHODS

In a cross-sectional study, 66 adults with CAP hospitalized in Alzahra Hospital (Isfahan, Iran) during 2011 were evaluated. CAP was defined as an acute illness occurring in a patient with clinical findings including fever, chills, cough, sputum production,

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Received: 17.11.2011; **Revised:** 14.12.2011; **Accepted:** 24.01.2012

dyspnea, pleuritic chest pain, and new pulmonary infiltrates on admission chest radiography.^[2] In order to perform Gram-stained smear and culture, sputa were collected from all patients at the time of admission before initiation of antibiotics. Urinary antigen test was also conducted on all participants. According to the results of the tests, 33 patients with positive Gram-stained sputum, indicative of pneumococci, with large numbers of Gram-positive cocci in pairs and chains and positive sputum culture for SP were considered as the case group. Subjects with positive results in both tests were regarded as pneumococcal pneumonia patients. Another 33 patients with the abovementioned symptoms and signs of pneumonia and with negative Gram-stained sputum and negative sputum culture were considered as the control group. Sputum was cultured using a standard microbiological method based on which a positive sputum culture result is one that yields SP on 5% sheep blood agar or 5% sheep blood agar containing Coly-Mycin and nalidixic acid after overnight incubation at 37°C under 5% CO₂.^[5] All samples including urine samples were collected from all patients at time of admission. Individuals with no sputum or antibiotic use were excluded from the study. BinaxNOW® (Inverness Medical, Cologne, Germany) was used to perform ICT on non-concentrated urine. According to the manufacturer's instructions, test results were read and interpreted as positive, negative and invalid (sample line only or no line) at 15 minutes.

After collecting the data, statistical analyses were per-

formed using MedCalc_{11.6}. Variables were expressed as mean ± standard deviation (SD). Student's t- test was used to compare variables. Statistical significance was defined as $p < 0.05$.

RESULTS

All 66 samples were included in the analyses (33 samples with positive and 33 with negative sputum smear and culture). The mean age of patients was 52.13 ± 23.09 years. Moreover, 47 (71.2%) patients were male and 19 (28.8%) were female. Pneumococcal urinary antigen test results were negative in all patients with negative sputum smear and culture. Out of 33 patients with positive sputum smear and culture, 23 patients showed positive urinary antigen test while 10 had negative urinary antigen test. Table 1 presents the characteristics of patients and results of urinary antigen test based on sputum smear results. The mean age of patients with positive sputum smear and culture (55.44 ± 18.55) was more than the other group (48.41 ± 19.07) ($p = 0.14$). In addition, there was a statistically significant difference in urinary antigen test results between patients with positive and negative sputum smear and culture ($p < 0.0001$). As shown in table 2, the sensitivity of urinary antigen test for diagnosis of pneumococcal pneumonia in patients with positive sputum smear and culture was 69.70%. On the other hand, the specificity of urinary antigen test for detection of pneumococcal pneumonia in patients with negative sputum smear and culture was 100%.

Table 1. Characteristics and results of urinary antigen test based on sputum smear and culture results

	Pneumococcal pneumonia group (n = 33)	Non-pneumococcal pneumonia group (n = 33)	p
Age (year)	55.44 ± 18.55	48.41 ± 19.07	0.14
Male	27 (81.8%)	20 (60.6%)	
Female	6 (18.2%)	13 (39.4%)	0.1

Data is presented as mean ± SD or number (percent). P-values were calculated by independent-t and chi-square tests with Yates correction for continuity.

Table 2. Diagnostic indices of urinary antigen test in patients with pneumococcal pneumonia

	Percentage	95% CI
Sensitivity	69.70%	51.29-84.38
Specificity	100%	89.32-100
Positive predictive value	100%	85.05-100
Negative predictive value	76.74%	61.36-88.23

DISCUSSION

SP has been recognized as the most common cause of CAP in adults^[12] and the second most frequent cause of bacterial meningitis as well as a prevalent cause of bacteremia.^[13] In this study, we evaluated the sensitivity and specificity of pneumococcal urinary antigen test for distinguishing between patients with and without pneumococcal pneumonia among CAP patients. For this purpose, we used an ICT (BinaxNOW®, Inverness Medical, Cologne, Germany) which could detect pneumococcal C polysaccharide cell wall in urine samples of patients.^[11,14] We evaluated 66 samples in the analysis (33 with positive and 33 with negative sputum smear and culture). Among the patients with positive sputum smear and culture, 23 persons had positive and 10 had negative urinary antigen test results. All patients with negative sputum smear and culture had negative urinary antigen test results. The sensitivity and specificity of urinary antigen test in patients with positive sputum smear and culture were 69.70% (95% CI: 51.29-84.38) and 100% (95% CI: 89.32-100), respectively. According to the positive and negative predictive values of the test [100% (85.05-100) and 76.74% (61.36-88.23), respectively], the test can differentiate between patients with and without pneumococcal pneumonia. Our findings support previous studies. For instance, Ercis et al. reported urinary antigen test to have a sensitivity of 72.7%, a specificity of 97.6%, a positive predictive value of 88.9%, and a negative predictive value of 93%.^[15] Similarly, Genne et al. calculated the sensitivity and specificity of urinary antigen test in patients with pneumonia as 64.3% and 98.8%, respectively.^[16] In another study, Sorde et al. found urinary antigen test to have a specificity, positive predictive value, and positive likelihood ratio of 96%, 88.8-96.5%, 14.6-19.9, respectively. They thus concluded that the pneumococcal urinary antigen test was a useful tool in treatment of hospitalized adult CAP patients.^[17] Likewise, Dominguez et al. identified ICT, with a specificity of 97.2%, as a valuable tool for the diagnosis of pneumococcal pneumonia, especially in non-bacteremic cases.^[18] In another study on 220 non-severely immunosuppressed adults, Roson et al. confirmed the limited sensitivity (65.9%; 95% CI: 51.4-80.4) but high specificity (100%; 95% CI: 99.7-100) of ICT for diagnosing pneumococcal pneumonia.^[19]

We demonstrated urinary antigen test to be sensitive and highly specific. However, some limitations in our study made our results a little different from, but still consistent with, other studies. First, our sample size was smaller than similar studies. Second, we did

not classify patients based on disease severity. Therefore, we could not establish a relationship between positive urinary antigen and severity of the disease. However, a small sample size would result in low sensitivity and positive predictive values. At the end, we can conclude that ICT is a sensitive and highly specific method for diagnosis of pneumococcal pneumonia. It can thus be used as a suitable complementary method for rapid screening of urine samples. Nevertheless, it must be accompanied by culture and Gram-stained smear for determining the etiology of CAP in adults.

ACKNOWLEDGMENTS

This paper is derived from a specialty thesis in Isfahan University of Medical Sciences. We gratefully acknowledge Dr M. Yaran for his incorporation in microbiological diagnosis through providing proper culture media for pneumococci growth. Authors also thank Dr. Sahar Emami Naeini for her invaluable help in preparing this manuscript.

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How to cite this article: Emami Naeini A, Ataei B, Shirani K, Akbari M. Assessment of a urinary antigen test in inpatients with pneumococcal pneumonia. *J Res Med Sci* 2012; 17(Spec 2): S182-S185 .

Source of Support: This research was supported by a grant from Isfahan University of Medical Sciences, Isfahan, Iran., **Conflict of Interest:** None declared.