Respiratory Medicine (2010) **104**, 397–403

available at www.sciencedirect.com

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journal homepage: www.elsevier.com/locate/rmed

Utility of pneumococcal urinary antigen detection in diagnosing exacerbations in COPD patients

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Received 20 December 2008; accepted 19 October 2009
Available online 5 November 2009

KEYWORDS
Chronic obstructive pulmonary disease (COPD);
Streptococcus pneumoniae;
Urinary antigen;
COPD exacerbation;
Immunochromatographic test;
Rapid diagnosis

Summary
The aim of this study was to evaluate the utility of pneumococcal urinary antigen detection (Binax Now *Streptococcus pneumoniae* Antigen Test) in diagnosing pneumococcal exacerbation of chronic obstructive pulmonary disease (COPD). Forty-six patients with *S. pneumoniae* isolation in sputum culture were studied (29 collected in stable period and 17 collected during exacerbation). In the 29 patients with samples collected in a stable period the antigen was detected in 3 cases (10.3%) using nonconcentrated urine (NCU), and in 12 cases (41.4%) using concentrated urine (CU). Regarding patients recruited during an exacerbation period, the antigen was detected in 3 cases (17.6%) using NCU, and in 13 cases (76.5%) when CU was used. For the evaluation of the specificity of the ICT test we also tested 72 cases in which pneumococcus was not isolated in the sputum sample. ICT was positive in 1 NCU and 9 CU of these patients. To have had at least one previous exacerbation ($P = 0.024$), at least one exacerbation that required hospitalization ($P = 0.027$), and a pneumonia episode in the year before ($P = 0.010$) had statistically significant associated with the detection of specific antigen in CU. Using NCU, the only significant association was found when a previous

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0954-6111/$ - see front matter
doi:10.1016/j.rmed.2009.10.013

pneumonia in the year before had occurred ($P = 0.006$). In summary, a positive result of pneumococcal urinary antigen from a COPD patient, in both bronchial exacerbation and pneumonia, should be evaluated with caution because the antigen detected could be related with previous infectious episode.

Introduction

Chronic obstructive pulmonary disease (COPD) is defined physiologically by the presence of irreversible or partially reversible airway obstruction in patients with chronic bronchitis and/or emphysema.[1] Some patients with COPD are prone to frequent exacerbations which are a major cause of morbidity and mortality and an important determinant of health related quality of life.[2–4] Bacteria cause a substantial proportion of exacerbations of COPD which cause considerable morbidity and mortality.[5–7] Bacteria are isolated from sputum in 40—60% of acute exacerbations of COPD. The three predominant bacteria species isolated are non-type *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Streptococcus pneumoniae*, although Gram negative enteric bacilli, and *Pseudomonas* spp are also frequently isolated in patients with severe COPD.[8] Several new lines of evidence demonstrate that bacterial isolation from sputum during acute exacerbation in many instances reflects a cause-effect relationship.[4]

Cultures of expectorated sputum from adults experiencing exacerbations of COPD reveal that *S. pneumoniae* is isolated from 7 to 26% of such samples. However, prevalence studies reveal that 20—40% of stable COPD patients are colonized at any time by this microorganism.[7,9,10] Therefore, the isolation of *S. pneumoniae* from sputum samples of chronic bronchitis patients only provides a probable etiological diagnosis of the exacerbation. In addition, pneumococcus is not usually isolated from the blood culture during exacerbation. At the moment, a reliable method to distinguish between colonization and clinical infection in COPD patients does not exist.

In the last years, a new immunochromatographic (ICT) test (Binax Now *S. pneumoniae* Antigen Test, Portland, Maine, USA) was developed for detecting polysaccharide C (PnC) in urine samples[11–13] as well as serum[14] and pleural fluid samples.[15] The test has proven rapid, sensitive and specific in diagnosing pneumococcal pneumonia in adults.[11,12,16] Furthermore, concentrating the urine by selective ultrafiltration may elevate the utility of this test because it increases sensitivity.[17,18] The introduction of a *S. pneumoniae* urinary antigen assay in clinical practice has increased the rate of the etiological diagnosis of pneumococcal pneumonia.[18]

The aim of this study was to assess the performance of the ICT method in diagnosing the pneumococcal bronchial exacerbation of COPD, detecting specific urinary antigen.

Methods

Group of patients

We recruited prospectively COPD patients who attended to Hospital Universitari Germans Trias i Pujol (Barcelona, Spain) and Hospital de Sant Boi de Llobregat (Barcelona, Spain) for routine outpatients visits during a stable COPD period, or for exacerbation of the disease. All patients met standard criteria for the diagnosis of COPD.[1] Ethics approval for this study was provided by the Ethics Committee of the Hospital Universitari Germans Trias i Pujol, and of the Fundació Jordi Gol i Gurina (Barcelona. Spain). The severity of the disease was established by means of the forced expiratory volume in one second (FEV_1) following the standard recommendations for the diagnosis and treatment of patients with COPD.[19] The clinical diagnosis of COPD exacerbation was defined as increased breathlessness, and/or increased sputum volume, and/or new or increased sputum purulence.[20]

Patients included in the study were analysed into groups according to the fact that they were recruited during an exacerbation or during a stable period of the disease, and on the basis of the result of the sputum culture. Urine samples were collected for *S. pneumoniae* antigen detection, being frozen at $-20\,^{\circ}C$ until testing.

The characteristics recorded for the patients included in the study were the following: age, gender, smoking status, underlying diseases, cor pulmonale, years since evolution of COPD symptoms, basal dyspnoea, FEV_1, clinical symptoms, chest radiograph findings, microbiological results, home oxygen therapy, and prior antibiotic and/or steroid treatment. It was also recorded the number of exacerbations and the number of exacerbations that required hospitalization during the previous year, the occurrence of a previous pneumonia episode, and antibiotic treatment. The basal treatment for COPD and information about the evolution of the disease were also recorded.

Patients that needed hospitalization to treat their exacerbation followed conventional treatment based on bronchodilators agents, systemic steroids, antibiotics and oxygen therapy.

Inclusion criteria

COPD patients with $FEV_1 < 80\%$ after bronchodilators agents, and/ airflow obstruction as evidenced by a ratio of FEV_1 to forced vital capacity (FVC) < 0.70 were included in the study.

Exclusion criteria

The exclusion criteria were the following: patients with clinical or radiological evidence of pneumonia at the moment of diagnosis, or with documented pneumonia in the previous two months, or with new chest radiographic infiltrates in the following 48 h. Patients with history of asthma, lung cancer causing airway obstruction, or other significant respiratory disease, including active tuberculosis; patients vaccinated against *S. pneumoniae* within the