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Antibiotic treatment and the diagnosis of *Streptococcus pneumoniae* in lower respiratory tract infections in adults

Jens Korsgaard [a,*], **Jens K. Møller** [b], **Mogens Kilian** [c]

[a] *Department of Chest Diseases, Aarhus University Hospital Aalborg, DK-9000 Aalborg, Denmark*
[b] *Department of Clinical Microbiology, Aarhus University Hospital Skejby, DK-8200 Aarhus N, Denmark*
[c] *Institute of Medical Microbiology and Immunology, University of Aarhus, DK-8000 Aarhus C, Denmark*

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Summary

Objective: To analyze the possible influence of antibiotic treatment on the results of different diagnostic tests for the diagnosis of lower respiratory tract infections with *Streptococcus pneumoniae*.
Material and methods: A prospective cohort of 159 unselected adult immunocompetent patients admitted to Silkeborg County Hospital in Denmark with community-acquired lower respiratory tract infections underwent microbiological investigations with fiber-optic bronchoscopy with bronchoalveolar lavage, blood and sputum culture and urine antigen test for type-specific polysaccharide capsular antigens of *S. pneumoniae*.
Results: When stratified for antibiotic treatment prior to microbiological sampling, three different groups of patients with documented or probable infection with *S. pneumoniae* could be identified. The first group comprised 14 patients who were culture positive in one or more culture tests, where most (11/14) did not receive any antibiotic treatment within 24 hours of sampling. The second group consisted of nine patients with a positive urine antigen test where 8/9 and 9/9 received antibiotic treatment 24 and 48 hours, respectively, prior to urine sampling. Only a single patient was positive in both systems, making a total of 22 patients with documented pneumococcal infection. As a positive culture test was dependent on the absence of antibiotic treatment, whereas a positive urine antigen test depended on antibiotic treatment within 48 hours, the two tests were complementary in the diagnosis of infection with *S. pneumoniae*. The third group of patients with probable pneumococcal infection were identified as 26% and 20% of the remaining 137 patients with

* Corresponding author. Tel.: +45 87 22 23 60; fax: +45 86 80 24 40.
E-mail address: j.korsgaard@dadlnet.dk (J. Korsgaard).

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unknown or known non-pneumococcal etiology, respectively, who received recent antibiotic treatment within 2–4 weeks of diagnostic sampling. By comparison, 0% ($p < 0.01$) with documented pneumococcal infection received antibiotic treatment in weeks 2–4 prior to microbiological sampling. As such a further eight patients should be expected to have infection with *S. pneumoniae* but would test negative in both culture tests and the urine antigen test because of antibiotic treatment within weeks 2–4 prior to sampling.

Conclusion: The diagnosis of infection with *S. pneumoniae* is very dependent on whether or not recent (within 2–4 weeks) or immediate (within 48 hours) antibiotic treatment has been given prior to microbiological sampling of patients. The results suggest an optimized diagnostic strategy with, if possible, sampling for culture prior to antibiotic treatment, while sampling for pneumococcal antigens should wait 24–48 hours for antibiotic treatment.

Introduction

Infection with *Streptococcus pneumoniae* is the most frequently reported etiology in lower respiratory tract infections (LRTI) with frequencies from 29%[1] to as high as 48% in a recent British survey.[2] The diagnostic approach in pneumococcal disease is difficult, as blood culture is very specific but lacks sensitivity, and sputum culture may represent colonization as 30–70% of adults with chronic obstructive pulmonary disease are colonized with *Streptococcus pneumoniae*.[3] More invasive investigations with fiberoptic bronchoscopy improve the diagnostic yield but seem only justified as a routine diagnostic procedure in patients with severe disease.[4] Furthermore, the prior administration of antibiotic treatment before sampling bacteriological material clearly reduces the frequency of culture of pneumococci. For example, 42% of patients with severe community-acquired pneumonia without prior antibiotic treatment became culture positive, in contrast to only 15% of patients treated with antibiotics before microbiological sampling.[5]

This difficulty in the diagnosis of pneumococcal infection is one of the reasons for the assumption[6] that it is the most frequent etiology, even among patients with no etiologic diagnosis despite comprehensive microbiological sampling. It is also the reason for the continued search for new and better diagnostic methods in pneumococcal disease. Among the latter are several methods to detect either type-specific polysaccharide capsular antigens (PCA) or to detect C-polysaccharide from the pneumococcal cell wall. These antigens can be detected in sputum, blood or urine samples. These methods have been tested in several investigations, where results show a generally high (above 90%) diagnostic specificity, but diagnostic sensitivity is variable and often low, so that half or more of patients with proven pneumococcal disease by culture remain negative for urine antigen.[7] Thus no antigen detection tests have proved to be sufficiently effective to gain a place in the routine diagnosis of respiratory infection.[8,9]

This study was designed to validate culture for *S. pneumoniae* and urine antigen detection of capsular antigens in adult patients admitted to hospital with lower respiratory tract infection in relation to the administration of antibiotic treatment prior to microbiological sampling.

Material and methods

A total of 159 immunocompetent unselected adult patients admitted to Silkeborg County Hospital in Denmark from 1 September 1997 to 1 September 2000 with lower respiratory tract infections were consecutively included in the study, while eight patients fulfilling the inclusion criteria declined participation. The clinical diagnosis of LRTI required that the patient had fever (rectal temperature $\geq$37.6 °C within 48 hours of inclusion in the study) and/or an increased leucocyte count ($\geq 11 \times 10^9$/l) in peripheral blood on admission as signs of inflammation, together with increased focal symptoms from the lower airways with at least one of three newly developed symptoms of increased dyspnoea, increased coughing and/or increased sputum purulence.[10] Of the 159 patients diagnosed with lower respiratory tract infections 89 (56%) appeared with a new infiltrate on their chest X-ray on admission, while 70 were without new infiltrates. All patients were admitted with community-acquired infection and were investigated within 24 hours of admission.

Patients with known malignancy and patients with an oxygen saturation below 85% with a maximum of 1 litre nasal oxygen prior to possible