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Institutionen för Medicin, Enheten för Infektionssjukdomar, Karolinska Institutet, Stockholm

Aetiology in community-acquired pneumonia

AKADEMISK AVHANDLING

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ABSTRACT

Background: Although community-acquired pneumonia (CAP) is a common and well-known disease, its microbial aetiology is still not well characterized. During the past few years nucleic acid detection using real-time polymerase chain reaction (PCR) has been developed for detection of many bacterial and viral pathogens causing respiratory tract infections.

Objectives: 1) to estimate the accuracy of the quantitative real-time PCR (RQ-PCR) method for identifying pneumococci in sputum; 2) to determine the aetiology of CAP by implementing new diagnostic PCR techniques combined with conventional methods; 3) to compare CAP patients with a pure bacterial aetiology with those with both bacterial and viral findings regarding severity of illness and length of hospital stay; 4) to study the inflammatory response, especially procalcitonin (PCT) levels, in patients with CAP and the correlation to different respiratory pathogens.

Material and methods: Adults admitted to Karolinska University Hospital were studied during a 12-month period. All patients were tested with an extensive panel of conventional methods and in addition sputum samples were analysed with RQ-PCR for *Streptococcus pneumoniae, Haemophilus influenzae,* and *Moraxella catarrhalis*; and nasopharyngeal specimens were analysed with real-time PCR for viruses common in the airways. Serum samples were collected within 24 hours of admission for subsequent measurement of PCT, C-reactive protein, transthyretin and interleukin-6. The pneumonia severity index (PSI) was used to assess the severity of illness.

Results: In sputum samples, culture was significantly positive in 19/128 (15%), whereas a significant concentration of DNA was found with RQ-PCR in 34/127 (27%) cases ($p < 0.001$). Seventeen of the 34 RQ-PCR–positive sputum samples were negative by sputum culture, of which 14 were from patients treated with antibiotics prior to sampling. A microbial aetiology was found in 67% of all patients (n=124). The most frequently detected pathogens were *S. pneumoniae* (70 patients [38%]) and respiratory virus (53 patients [29%]). Multiple pathogens were present in 43 (35%) of those with a determined aetiology. The likelihood of getting a score corresponding to PSI classes IV or V was higher in patients with combined bacterial-viral findings than in those with a bacterial pathogen alone (odds ratio 4.98, 95% confidence interval 2.09 – 11.89; $p < 0.001$). The median length of hospital stay was seven days among patients with mixed infections and four days among those with a bacterial aetiology alone (p=0.018). Median serum concentrations of PCT were higher in patients with bacteraemia than in those without bacteraemia (6.11 µg/L vs. 0.34 µg/L, P=0.0002), in those with non-bacteraemic pneumococcal aetiology than in those infected with other classic bacteria (1.18 vs. 0.18, P=0.038), in patients with pneumococcal as compared to viral aetiology (2.43 vs. 0.24, P=0.017), and in patients with PSI classes 4-5 (2.07) than in those with PSI classes 1-3 (0.52, P=0.03).

Conclusions: The sensitivity of sputum RQ-PCR was higher than that of sputum culture, especially after antibiotic therapy had been initiated. By supplementing traditional diagnostic methods with new PCR-based methods, a high microbial yield was achieved. Mixed bacterial-viral infections were frequent and these patients developed severe CAP more often and stayed longer in hospital than those with a bacterial aetiology alone. High PCT seems to be a good marker of invasive as well as severe disease and of pneumococcal aetiology, but for localised bacterial infections caused by other pathogens the test is less sensitive.

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