Invasive Pneumococcal Infections

Akademisk avhandling

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av

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Avhandlingen baseras på följande delarbeten:

I Berg S, Trollfors B, Persson E, Backhaus E, Larsson P, Ek E, Claesson BE, Jonsson L, Rådberg G, Johansson S, Ripa T, Kaltoft MS, Konradsen HB.
Serotypes of Streptococcus pneumoniae isolated from blood and cerebrospinal fluid related to vaccine serotypes and to clinical characteristics.
Scand J Infect Dis. 2006;38 (6-7):427-32.

II Backhaus E, Berg S, Trollfors B, Andersson R, Persson E, Claesson BE, Larsson P, Ek E, Jonsson L, Rådberg G, Johansson S, Ripa T, Karlsson D, Andersson K.
Antimicrobial susceptibility of invasive pneumococcal isolates from a region in south-west Sweden 1998-2001.
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Pneumococcal clonal type affects disease outcome in humans.
Manuscript.

IV Backhaus E, Berg S, Andersson R, Ockborn G, Malmström P, Dahl M, Nasic S, Trollfors B.
Epidemiology of Invasive Pneumococcal Infections: Long-Term Trends in Incidence, Case Fatality Rate and Risk Factors in Children and Adults.
Manuscript.

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Abstract

Streptococcus pneumoniae is a major cause of disease, ranging from uncomplicated respiratory infections to severe invasive pneumococcal disease (IPD), including bacteraemic pneumonia, septicaemia with unknown focus and meningitis. Case fatality rate (CFR) remains high and antibiotic resistance is increasing globally. *Str. pneumoniae* is surrounded by a polysaccharide capsule that can be divided into more than 90 immunologically different serotypes. Vaccination may reduce morbidity and mortality due to IPD. Two vaccine types exist: pneumococcal polysaccharide vaccine (PPV-23) and pneumococcal conjugate vaccines (PCV-7, 10, 13). The former contains 23 serotypes, but does not work in small children, whereas the latter also protects children below two years of age, but includes only 7, 10 and 13 serotypes, respectively.

The aim was to explore the epidemiology of IPD before the introduction of PCV-7 in the Swedish childhood vaccination programme, in January 2009: serotype distribution, antimicrobial susceptibility and potential vaccine coverage among isolates causing IPD; mortality, case fatality rate and incidence of different IPD manifestations related to age and risk groups; the impact of serotype and genotype on manifestations and outcome; and finally, long-term changes in the epidemiology during 45 years.

Consecutive isolates and clinical data from 836 adults and children with IPD were collected in the Västra Götaland region (VGR) and Halland during 1998-2001. Serotype and antibiotic susceptibility were determined. Clonal complex (CC) was determined for these isolates together with 424 IPD isolates from adults and children in Stockholm using pulsed field gel electrophoresis (PFGE) and multi-locus sequence typing (MLST). Clinical data for all 2977 IPD episodes in VGR during 1996-2008 were retrieved from hospital notes. Prevalence data for predisposing factors were included from patient registries and recent publications.

Of 836 strains, 42%, 70%, 75% and 94% belonged to serotypes included in PCV-7, -10, -13 and PPV-23, respectively. Decreased susceptibility was uncommon, and largely confined to certain clones and serotypes, especially those included in PCV-7. Serotypes 1 and 7F were most common; they infected younger patients with less underlying disease and lower CFR than other serotypes, whereas 19A caused higher CFR. Clonal distribution differed between adults and children. CC306 (all serotype 1), caused lower CFR among adults than 6 other CCs. The relation between serotype and CC was complicated; clinical characteristics differed between some CCs within the same serotype and between some serotypes within the same CC; it was often difficult to determine whether these differences were related to serotype, CC or both.

The annual incidence of IPD was 15/100,000 and varied largely. It was highest at extremes of age and in patients with myeloma (2238/100,000), followed by chronic lymphatic leukemia, haemodialysis, lung cancer, HIV, rheumatic diseases, chronic obstructive pulmonary disease and diabetes mellitus. In contrast, it was not elevated among asthma patients. When compared with data from previous studies during 45 years, the incidence increased threefold and the CFR dropped from 20 to 10% for all IPD, whereas the incidence remained stable (1.1/100,000/year) and the CFR dropped from 33 to 13% for meningitis.

In conclusion, incidence and CFR have changed considerably over time and vary widely between different age and risk groups. CFR is also influenced by serotype and genotype. These factors have to be considered during planning and evaluation of vaccination programmes.

Keywords: *Streptococcus pneumoniae*, epidemiology, risk factors, pneumonia, meningitis, serotype, clonal complex.

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