Changing epidemiology of pneumococcal disease in the post vaccine era

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Until recently, the 7-valent pneumococcal conjugate vaccine (PCV7) has proved to be a great vaccine with an impressive effectiveness against multiple outcomes of pneumococcal disease. This included invasive pneumococcal diseases (IPD), pneumonia and otitis media. Furthermore, the reduction of nasopharyngeal carriage of the PCV7 serotypes resulted in the reduction of transmission of these serotypes, and thus, in the reduction in disease in contacts, including non-vaccinated individuals of all ages (termed “herd immunity”). In addition, some of the most antibiotic-resistant pneumococcal serotypes could be reduced or eliminated by PCV7. However, important needs are still unmet, and thus it is important to test whether the new generation extended spectrum PCVs (PCV10 and PCV13) can improve overall effectiveness against pneumococcal diseases. Several entities and conditions have shown less-than-expected effectiveness with PCV7. Pleuropneumonia has been found to be universally caused mainly by serotypes 1, 3, 5, 7F, 14 and 19A (of which only serotype 14 is a PCV7 serotype). Furthermore, pneumonia in general, mainly in older children, is often caused by serotypes not included in PCV7. In otitis media, serotypes such as 3, 6A and 19A are important. In addition, extensive antibiotic use has resulted in increased pressure and promotion of several antibiotic-nonsusceptible non-PCV7 serotypes, mainly 19A, but also 15 B/C, 35B, 6C and more. Thus, the combined pressure by antibiotic use on the one hand, and some replacement in nasopharyngeal carriage by PCV7 on the other hand, has resulted in increased carriage of and disease from some strains such as serotype 19A, 6C and a few others. Understanding the dynamics in pneumococcal carriage and disease, together with extensive variation with the new generation extended-spectrum vaccines on the one hand and reducing antibiotic pressure on the other hand, need to be emphasized to contribute to the success of reducing pneumococcal disease in children.

In vitro pneumococcal resistance: What does it mean in the clinical practice?

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Streptococcus pneumoniae remains one of the major pathogens in children and adults worldwide. In addition to the 100,000,000 ear infections in children, it is estimated that it is responsible for more than 5,000,000 pneumonia cases and approximately 100,000 meningitis cases, the whole being associated with 10,000,000 bacteremia cases every year. Mortality is still considerable, despite a wide battery of antibiotics. The mortality rate ranges from 6.4% among patients in an ambulatory and hospital setting to >40% among patients treated in an intensive-care unit. The ability of this bacterium to cause invasive disease is linked to multiple virulence factors. Over the past 3 decades, antimicrobial resistance among Streptococcus pneumoniae, the most common cause of community-acquired pneumonia (CAP), has escalated dramatically worldwide. In the late 1970s, strains of pneumococci displaying resistance to penicillin were described in South Africa and Spain. By the early 1990s, penicillin resistant clones of S. pneumoniae spread rapidly across Europe and globally.
Additionally, resistance to macrolides and other antibiotic classes escalated in tandem with penicillin resistance. Six international clones (serotypes 6A, 6B, 9V, 14, 19F, 23F) were responsible for most of these resistant isolates. The epidemiology of pneumococci is changing as different countries introduce the different conjugate pneumococcal vaccines. The introduction of the seven-valent pneumococcal conjugate vaccine (PCV7) in the 2000s and a reduction in antimicrobial use were associated with a significant decline in the incidence of invasive pneumococcal infections and in rates of antibiotic resistance in the USA. However, an increase in the incidence of infections caused by non-PCV7 serotypes, especially multidrug-resistant type 19A pneumococci, has been observed in many countries over the last 5 years. Currently, 15 to 30% of Streptococcus pneumoniae worldwide are multidrug-resistant (MDR) (i.e., resistant to 3 classes of antibiotics), exemplified by the recent appearance and spread of the 19A serotype. Despite the dramatic escalation in the rate of antimicrobial resistance among pneumococci worldwide, the clinical impact of antimicrobial resistance is difficult to define. Treatment failures due to antibiotic-resistant pneumococci have been reported with meningitis, otitis media, and lower respiratory tract infections, but the relation between drug resistance and treatment failures has not been convincingly established. Clinical failures often reflect factors independent of antimicrobial susceptibility of the infecting organisms. Host factors (e.g., extremes of age; underlying immunosuppressive or debilitating disease; comorbidities), or factors that affect intrinsic virulence of the organisms (e.g., capsular subtype) strongly influence prognosis. Tleyjeh et al. (as reviewed by Lode) reviewed ten studies out of 1152 articles that fulfilled their criteria. The authors examined the association between penicillin non-susceptible pneumococci and short-term mortality in pneumococcal pneumonia, and found a significant difference in the mortality rate (19.4% in the penicillin non-susceptible pneumococci group and 15.7% in the penicillin-susceptible S. pneumoniae group). They concluded that penicillin non-susceptibility is a prognostic factor and should be included as a risk factor for mortality. Prospective, randomized trials designed to assess the clinical significance of antimicrobial resistance among pneumococci are lacking. Does in vitro resistance translate into clinical failures? Should changing resistance patterns modify our choice of therapy for CAP or for suspected pneumococcal pneumonia? If clear answers are not to be available in the foreseeable future, then it is important to provide the best therapy for the treatment of this important infection using available clinical studies and pharmacokinetic/pharmacodynamics data, to minimize the occurrence of invasive disease with the use of vaccines, and to reduce or minimize the emergence and spread of resistant strains. Continued surveillance of antimicrobial resistance, serotypes and genotypes is crucial in providing information on the emergence of multiresistant clones. These data are also essential for the development of appropriate guidelines for empirical therapy of pneumococcal infections and for the inclusion of emergent serotypes in the new generation of conjugate vaccines.

Reference


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