Summary of WHO Position Paper on Pneumococcal conjugate vaccines in infants and children under 5 years of age, February 2019

This position paper, published in February 2019, replaces the corresponding WHO position paper on pneumococcal vaccines published in the Weekly Epidemiological Record in 2012. The focus of this position paper is use of pneumococcal conjugate vaccine (PCV) in infants and children < 5 years of age; a separate position paper on vaccination of older age groups with conjugate and polysaccharide vaccines will be developed after consideration by SAGE. The present position paper includes data on the effects of the 10- and 13-valent PCVs (PCV10 and PCV13) published up to June 2017 and specifically addresses the dosing schedule, product choice and the value of catch-up vaccination in children under 5 years of age.

Background

Pneumococcal infections can lead to serious invasive diseases such as meningitis, septicaemia and pneumonia, as well as milder but more common illnesses such as sinusitis and otitis media. There are > 90 known serotypes of S. pneumoniae. The distribution of serotypes that cause disease varies over time and by age, disease syndrome, disease severity, geographical region and the presence of antimicrobial-resistant genes. Of the estimated 5.83 million deaths among children < 5 years of age globally in 2015, 294 000 (uncertainty range [UR], 192 000–366 000) were estimated to be caused by pneumococcal infections. Before the introduction of pneumococcal conjugate vaccines (PCVs) in the different WHO regions, 6 – 11 serotypes accounted for ⩾ 70% of all invasive pneumococcal disease (IPD). The reported mean annual incidence of IPD in children aged < 2 years was 44.4/100 000 per year in Europe and 167/100 000 per year in the United States of America. In comparison, the annual incidence of IPD in children < 2 years in Africa ranged from 60/100 000 in South Africa to 797/100 000 in Mozambique. On average, about 75% of cases of IPD and 83% of cases of pneumococcal meningitis occur in children aged < 2 years, but the incidence and age distribution of cases may vary by country, study method and socio-economic status within countries. Case fatality rates from IPD in children can be high, ranging up to 20% for septicaemia and 50% for meningitis in low and middle income countries (LMICs).

Vaccines

Two polysaccharide-protein conjugate vaccines have been on the market since 2009: the 10-valent (PCV10) and the 13-valent (PCV13) vaccines. Previously, a 7-valent pneumococcal conjugate vaccine (PCV7) was available. Both PCV10 and PCV13 have been shown to be safe and effective and to have both direct (in vaccinated individuals) and indirect (in unvaccinated individuals living in communities with vaccinated children) effects against pneumococcal disease caused by vaccine serotypes when used in a 3-dose schedule (either 2p+1 or 3p+0) or in a 4-dose schedule (3p+1). After the third dose of each schedule (post-booster for 2p+1 and post-primary for 3p+0), the 2p+1 schedule resulted in higher geometric mean concentrations (GMCs) but a similar percentage of responders as compared with a 3p+0 schedule for most serotypes, except for serotype 6B, for which the percentage of responders was higher with the 2p+1 schedule.

Both PCV10 and PCV13 induce antibodies against the serotypes common to both vaccines (1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F). Although the mean antibody response to the common serotypes differed with the 2 products, in general, they induced comparable immunogenicity. PCV13 has 3 additional serotypes, 3, 6A and 19A. PCV13 induces an immune response to serotype 3; PCV10 contains neither serotype 3 nor any cross-reactive serotype, and immunogenicity against serotype 3 is not measured in studies of this vaccine. Both PCV10 and PCV13 induce an antibody response to serotype 6A, which is included in PCV13 but not in PCV10. Both PCV10 and PCV13 induce an antibody response against serotype 19A.

WHO Position

WHO recommends the inclusion of PCVs in childhood immunization programmes worldwide. Use of pneumococcal vaccine should be complementary to other disease prevention and control measures, such as appropriate case management, promotion of exclusive breastfeeding for the first 6 months of life and reducing known risk factors such as indoor air pollution and tobacco smoke.

For administration of PCV to infants, WHO recommends a 3-dose schedule administered either as 2p+1 or as 3p+0, starting as early as 6 weeks of age. In choosing between the 2p+1 and 3p+0 schedules, countries should consider programmatic factors, including timeliness of vaccination and expected coverage. The 2p+1 schedule has potential benefits over the 3p+0 schedule, when programmatically feasible, as higher antibody levels are induced in the second year of life, which may be important in maintaining herd immunity, although no high-quality evidence is available. If the 3p+0 schedule is used, a minimum interval of 4 weeks should be maintained between doses. If the 2p+1 schedule is selected, an interval of $\geqslant$ 8 weeks is recommended between the 2 primary doses, but the interval may be shortened if there is a compelling reason to do so, such as timeliness of receipt of the second dose and/or achieving higher coverage when a 4-week interval is used. The booster dose should be given at 9–18 months of age, according to programmatic considerations; there is no defined minimum or maximum interval between the primary series and the booster dose.

Previously unvaccinated or incompletely vaccinated children who recover from IPD should be vaccinated according to the recommended age-appropriate regimens. Interrupted schedules should be resumed without repeating the previous dose.

Both PCV10 and PCV13 have substantial impacts against pneumonia, vaccine-type IPD and nasopharyngeal (NP) carriage. There is at present insufficient evidence of a difference in the net impact of the 2 products on overall disease burden. PCV13 may have an additional benefit in settings where disease attributable to serotype 19A or serotype 6C is significant. The choice of product to be used in a country should be based on programmatic characteristics, vaccine supply, vaccine price, the local and regional prevalence of vaccine serotypes and antimicrobial resistance patterns. Once a PCV vaccination programme has been initiated, product switching is not recommended unless there are substantial changes in the epidemiological or programmatic factors that determined the original choice of product, e.g. an increasing burden of serotype 19A.

If a series cannot be completed with the same type of vaccine, the available PCV product should be used. Restarting a series is not recommended, even for the primary series.

Wherever possible, catch-up vaccination at the time of introduction of PCV should be used to accelerate its impact on disease in children aged 1–5 years, particularly in settings with a high disease burden and mortality.

PCVs should not be given to individuals with a history of anaphylactic reactions or severe allergic reactions to any component of the vaccine.

HIV-positive infants and pre-term neonates who have received their 3 primary vaccine doses before 12 months of age may benefit from a booster dose in the second year of life.

Travelling children are generally not at special risk of pneumococcal disease, unless they travel to an outbreak setting. They should follow the vaccine recommendations for the general population and ensure they are up to date with their vaccinations before travelling.

While a comprehensive surveillance system for pneumococcal disease is recommended, countries without such a system in place should not wait to introduce PCV vaccines.
WHO recommends that the epidemiological impact of PCV be carefully monitored in sustained, high-quality sentinel and population-based surveillance for pneumococcal disease and in periodic NP carriage surveys.

Additional research should be conducted on: (1) further assessment of vaccine impact, duration of protection and indirect effects of different dosing schedules; (2) serotype replacement; (3) further establishment of serotype-specific immune correlates of protection against IPD in different transmission settings; (4) the epidemiology of pneumococcal outbreaks, particularly epidemics of serotype 1 disease, including use of PCV to prevent or respond to outbreaks; (5) the impact of PCV on antimicrobial use and resistance; and (6) comparison of a 1-dose versus a 2-dose catch-up schedule for children > 12 months of age.