Editorial

Can infant vaccination prevent pneumococcal meningitis outbreaks in sub-Saharan Africa?

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Word count text and references = 1296

The WHO Strategic Advisory Group of Experts is reviewing the technical evidence to inform policy on optimal use of infant pneumococcal conjugate vaccines (PCV)(1). Since 2010, multivalent vaccines (PCV-10, PCV-13) have been successfully introduced with the support of Gavi the Vaccine Alliance into infant immunisation programmes across the developing world(2). One recommended schedule consists of three doses under the age of 6 months (3+0), with the aim of providing maximum protection to infants, the age group at highest risk of pneumococcal disease(3). An alternative schedule consists of two vaccine doses under the age of six months with a booster at 9-15 months (2+1). This schedule may have more impact on reducing carriage and transmission of vaccine serotypes to unvaccinated individuals, leading to indirect or herd protection. The question around the most cost effective policy to achieve both direct and indirect protection has particular importance for the meningitis belt of sub-Saharan Africa.

The launch of mass campaigns with a serogroup A conjugate vaccine (MenAfriVac^{R}) across the meningitis belt in 2010 saw a dramatic fall in the incidence of meningitis due to serogroup A, while meningitis due to other meningococcal serogroups and *Streptococcus pneumoniae* have become more prominent(4). Recent publications from the meningitis belt emphasise the continuing burden of pneumococcal meningitis among older children and adults in this region. In Ghana, a large outbreak occurred in 2016 with close to 900 suspected cases and 104 cases confirmed as due to *S.pneumoniae,* mainly serotype 1, with a median age of 20 years, in part of the country adjoining the meningitis belt(5). In Burkina Faso from 2011-13, 1,528 (53%) of 2,858 cases of laboratory confirmed bacterial meningitis were due to *S.pneumoniae,* also mainly serotype 1(6). The proportion of cases aged over 5 years was 95% in Ghana and 69% in Burkina Faso. PCV programmes that started in 2013 in

Ghana likely protected young children in the 2016 outbreak, whereas the Burkina Faso data were taken from the years preceding PCV vaccination.

Bacterial meningitis due to *S. pneumoniae* has a remarkably high case fatality ratios in Sub-Saharan Africa(7) and causes much disability in survivors(8). A systematic review of paediatric meningitis in children in Africa found among cases of confirmed pneumococcal meningitis that the median in-hospital case fatality ratio was 35% and that 25% of survivors had in-hospital sequelae, these figures being 9x and 4x higher respectively than those for meningococcal meningitis(8). Incidence of pneumococcal meningitis is particularly high in the meningitis belt, with a similar seasonality to meningococcal meningitis, consistent with similar predisposing environmental factors(7, 9). Reducing the burden of pneumococcal meningitis in these countries should be given high public health priority.

For outbreak control, pneumococcal vaccines could potentially be given to children and adults in reactive mass campaigns, a similar strategy to that using meningococcal vaccines for controlling outbreaks of meningococcal meningitis(10). However, reactive vaccination for meningococcal meningitis is resource intensive and relatively ineffective unless undertaken promptly (11, 12) and effectiveness of such a policy in controlling outbreaks of pneumococcal meningitis is not known(13). Preventive vaccination offers more hope. Even though serotype 1 is rarely found in carriage isolates, evidence of indirect protection against serotype 1 was found in South Africa after introduction of a 2+1 PCV-13 infant vaccination schedule (14).

How best can we achieve indirect protection of older age groups at high risk of pneumococcal meningitis in the meningitis belt? Inclusion of a booster dose may be more important for some serotypes, including serotype 1(15), and extended vaccination among

children up to the age of 5 years, in whom carriage prevalence is highest in sub-Saharan Africa(16), may increase effectiveness(2, 17). A 3+0 schedule supplemented by a catch up campaign to the age of 5 years in Kenya reduced carriage of vaccine serotypes in vaccinated and unvaccinated age groups(18). In contrast, a study from the Gambia showed no evidence as yet of a reduction in serotype 1 disease in persons aged >5 years after introducing a 3+0 PCV-13 schedule without catch up in 2011(19), and the pneumococcal meningitis outbreak this year in Ghana occurred despite the prior introduction of a 3+0 schedule with high coverage in the two previous years. Most countries of the meningitis belt have introduced a 3+0 schedule. Switching to a 2+1 schedule with a single dose catch up in children up to 5 years of age could extend individual protection, lead to a higher level of indirect protection and lower the risk of outbreaks from this devastating disease.

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