Correspondence

Pneumococcal Polysaccharide Vaccine Efficacy and Routine Use of Conjugate Vaccines in Infants: There Is No Need for a Vaccine Program in Older Adults at Present

To the Editor—The recent commentaries from Paradiso, Grabenstein, and Musher [1–3] demonstrate that the controversy surrounding efficacy of pneumococcal vaccination in older adults is fueled by polarized viewpoints. The licensing of the 13-valent pneumococcal conjugate vaccine (PCV13) in adults has meant that the debate on the relative merits of pneumococcal polysaccharide and conjugate vaccine now has to be realized by policy makers and clinicians.

We concur with the view expressed by Grabenstein that, at least in populations where infants have been fully immunized with PCV13 at high coverage rates, disease caused by the serotypes contained in the infant vaccine are likely to decline and eventually disappear in the population as a result of herd immunity. Logically, once these serotypes no longer cause disease in the elderly as a result of this indirect protection, there is little purpose in vaccinating them with the same costly vaccine. The almost complete disappearance of 7-valent pneumococcal conjugate vaccine (PCV7) serotypes among disease isolates in the over-65 age group and the continuing decline in PCV13 serotypes in populations with effective infant programs provide strong support for this perspective [4–6]. Where uptake of infant programs is lower and thus impact on carriage is incomplete [7], direct protection of the elderly with PCV13 may be a reasonable approach. As there are currently no data on PCV efficacy or effectiveness in this population, such an intervention could only be supported by extrapolation from a single trial of PCV in profoundly immunocompromised young adults infected with the human immunodeficiency virus in Malawi [8], or from data on the 23-valent plain polysaccharide vaccine (PPV23).

For this reason, it is important to examine the efficacy and effectiveness of PPV23, on which all 3 commentary authors reflect. There has been a series of meta-analyses published but the results are conflicting. The primary problem with the PPV23 literature is that there are no studies that adequately address the vaccine’s efficacy in the healthy 65-year-old community-dwelling population in a contemporary high-income setting. The 2008 Cochrane meta-analysis [9] attempted to resolve this issue using subanalyses of efficacy in high-income settings. Four studies were identified showing an overall efficacy of 74% (95% confidence interval [CI], 56%–85%) against invasive pneumococcal disease (IPD) with a study published by Kaufman in 1947 [10] having the greatest effect on this result. However, that study used 2- and 3-valent vaccines, not PPV23, and the populations studied were institutionalized adults >40 years of age in New York. Two other studies that were included used 12- and 14-valent vaccines given to adults of undefined age recruited from the Kaiser Permanente Health Plan and to 55–85-year-old adults living in hospices or retirement homes in France, respectively [11, 12]. Only 1 study examined the current PPV23, although this study recruited 50–85-year-old adults with a prior history of pneumonia. Although the overall efficacy is compelling, the extrapolation needed to support PPV23 from these studies using the wrong vaccine in the wrong population in a previous era is not comfortable. Furthermore, in the Cochrane review, there was no support from these studies for efficacy against pneumonia or all-cause mortality using any of these polysaccharide vaccines. Similarly, in a subanalysis in high-risk groups, those in greatest need of protection from Streptococcus pneumoniae, there was no evidence of efficacy against IPD or pneumonia or an effect on mortality. An additional problem with a program of immunization at 65 years of age is that morbidity from pneumococcal disease increases substantially with age thereafter. However, no studies have adequately addressed the impact of the vaccine for more than a few years after immunization.

Because there are so few data on the efficacy of PPV23 and given that the vaccine has been widely used, postlicensure surveillance data might be expected to provide clear evidence of effectiveness but do not. Data from the UK reveal a vaccine effectiveness of 48% (95% CI, 32%–60%) against IPD in persons aged >65 years for 2 years following vaccination, which wanes rapidly, being 21% (95% CI, 3%–36%) between 2 and 5 years and 15% (95% CI, −3%–30%) >5 years postvaccination [13]. Vaccine effectiveness was less in some clinical risk groups compared to healthy populations and in older compared with younger age cohorts in the population >65 years of age. One of the reasons for this short-lived protection after immunization may be loss of the memory B-cell pool after
PPV23 immunization, not observed following PCV7 immunization [14]. These data do suggest that PPV23 has some limited impact on IPD for a few years after vaccination, but less in those with chronic illness and no measurable impact on pneumonia or mortality. It may still be useful to vaccinate adults at 65 years of age to provide some short-lived protection (perhaps only until they reach around 67 years of age) if the vaccine is cheap enough. However, the cost-effectiveness analyses should take account of the impact of routine infant PCV13 immunization on PPV23 effectiveness and demonstrate that “covering” the 10 serotypes in PPV23, which are not included in PCV13, has an additional benefit.

A better strategy to protect older adults may be to develop a new vaccine that covers the serotypes affecting this age group in the post-PCV13 era, including those serotypes that are emerging as the major cause of IPD, for example, those in the United Kingdom in the period 2008–2010 (ie 22F, 33F, 16F, 23A, 35F, or 38; Figure 1). The success of such a strategy depends on maintenance of herd immunity provided by the infant conjugate vaccine program and will also need evidence of direct protection from conjugate vaccines in the elderly, which is not yet available.

Figure 1. Adjusted number of cases caused by 23-valent plain polysaccharide vaccine—only serotypes that are not included in 13-valent pneumococcal conjugate vaccine and the serotypes that are not covered by any current vaccine (nonvaccine serotypes) in the >65-year-olds in the pre—7-valent pneumococcal conjugate vaccine (PCV7) vaccine era (black bars) compared to the post—PCV7 vaccine era (gray bars). Numbers of cases are taken from Miller et al [15]; arrows indicate emerging serotypes. Abbreviations: PCV7, 7-valent pneumococcal conjugate vaccine; PPV23, 23-valent plain polysaccharide vaccine.

Notes

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