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Commentary on Evidence Summaries

The evidence for the use of pneumococcal polysaccharide vaccine to prevent invasive pneumococcal disease in adults and its implications for the developing world

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ABSTRACT

The pneumococcal polysaccharide vaccine was effective in preventing invasive pneumococcal disease in healthy adults, as well as both culture-confirmed and presumptive pneumococcal pneumonia. The present review offers the best evidence so far on the benefit of the vaccine, which is already recommended for use in industrialized countries for those at risk of pneumococcal infection and its complications. In the resource-limited setting with competing public health priorities, introduction of the polysaccharide vaccine faces several obstacles including the absence of data on disease burden and cost-effectiveness. Pneumococcal polysaccharide vaccine may be offered to those at risk while decisions are made on the best possible strategies for preventing pneumococcal disease in this population.

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1. The importance and relevance of this review in general

The 2013 Cochrane review by Moberley, Holden, Tatham and Andrews is the most recent of several systematic reviews and meta-analyses dating back from Fine in 1994 to Huss in 2009 on the benefit of pneumococcal vaccination in adults, and is an update of the authors' own Cochrane Review of 2008. The primary objective of the study was to assess the efficacy of pneumococcal polysaccharide vaccine (PPV) in preventing invasive pneumococcal disease (IPD), all-cause pneumonia

and mortality in various adult populations including those from low-income countries.¹

Previous meta-analyses have often shown conflicting results while answering these questions, due to various reasons including heterogeneity of included studies, the heterogeneity of all-cause pneumonia itself (with the diagnosis of presumed pneumococcal pneumonia based on a case definition without an identified pathogen from a sterile body site), as well as the small number of events such as mortality in most included studies. Studies where PPV is assessed against more specific objectives such as vaccine-serotype IPD tend to show the best

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results with regards to efficacy of pneumococcal polysaccharide vaccination in adults. With this in mind, the secondary objectives that were also analysed in this review were the efficacy of PPV against vaccine serotype-specific IPD, definitive and presumptive pneumococcal pneumonia, and mortality due to pneumonia and pneumococcal infection.

The authors found that PPV was efficacious in preventing all IPD with a vaccine efficacy of 74% (11 RCTs, 36489 subjects). PPV was also effective in preventing IPD in healthy adults in high-income countries (5 RCTs, 27886 participants) and healthy adults in a single trial in a low-income country (Papua New Guinea, 5373 subjects) where the subjects were considered to be at high risk of pneumococcal infection due to environmental factors such as overcrowding. PPV did not, however, show protective efficacy against IPD in adults with chronic disease in high-income countries due to a lack of power to demonstrate a significant difference between the vaccinated and control groups. PPV did not demonstrate efficacy against all-cause mortality or pneumonia-related mortality. Although PPV was not demonstrably useful in preventing mortality due to pneumococcal disease due to the small number of such events, it was beneficial in preventing IPD due to vaccine-specific serotypes, as well as both definitive (culture-confirmed) and presumptive pneumococcal pneumonia.

Pneumococcal infections are estimated to cause 30–50% of community-acquired pneumonias in Europe and the United States. Data from industrialized countries shows an incidence of invasive pneumococcal disease ranging from 24 to 85 per 100,000 population in adults aged 65 years and older.² Accordingly, many industrialized countries recommend vaccination with pneumococcal polysaccharide vaccine for all people ≥ 65 years of age and for those aged 19–64 years with underlying conditions that put them at increased risk for pneumococcal infection and serious complications of pneumococcal infection, such as chronic heart, lung or liver disease, diabetes mellitus, alcoholism and cigarette smoking. For other high-risk groups such as those with malignancy, congenital or acquired immunodeficiency or immune suppressive medication, chronic renal disease, functional or anatomic asplenia, cochlear implants or solid organ transplants, the American Advisory Committee on Immunization Practices (ACIP) recommends a dose of pneumococcal conjugate vaccine (PCV) 8 weeks prior to PPV,³ with PCV acting to prime the immune system to elicit a boosted antibody response to PPV (although consistent evidence on the benefit of this strategy is lacking⁴). The present review supports the use of PPV to prevent invasive pneumococcal disease in adults.

2. The relevance of this review to the developing world

Data on invasive pneumococcal disease from the developing world is less robust, and in the absence of national surveillance systems is available mainly from hospital-based surveillance. Data from seven tertiary care hospitals in India over a 15-year period from 1993 to 2008 documented a case fatality rate of 25–30% in older adults with IPD, and that over 80% of the serotypes responsible for invasive pneumococcal disease are included in the formulation of PPV.⁵ While this confirms

the severity of IPD and potential benefit of PPV in its prevention, actual data on the incidence of IPD in India is not available. In a country with competing priorities in public health, an essential pre-requisite for introduction of PPV in a targeted population would be community-based surveillance to document the burden of disease in that population followed by mathematical modelling to assess the cost-effectiveness of such an intervention.

A position paper by the World Health Organization suggests that, in resource-limited settings, a higher priority would be introducing and maintaining a high coverage of PCV in infant immunization programs,² given the substantial herd immunity evidenced in adults following routine PCV immunization in infants (with equal reduction in IPD, pneumococcal pneumonia and mortality among both vaccinated children and unvaccinated adults⁶). When one considers the fact that functional antibody responses to PPV are age-dependent, being lower in the elderly compared to younger adults, as well as showing poor persistence in some studies this does appear to be a more viable option in a country such as ours. Although pneumococcal conjugate vaccine is recommended by the Indian Academy of Pediatrics as part of the primary vaccination schedule from infancy,⁷ the high cost of PCV in the private sector plus the fact that it is not part of the national Universal Immunization Programme (UIP) makes adequate infant coverage for the benefit of adult herd immunity unlikely in the immediate future. However, the introduction and scaling up of pentavalent vaccine with support from the GAVI Alliance, along with the Government of India's recent decision to introduce IPV, rotavirus, rubella into the UIP as well as Japanese encephalitis vaccine in endemic areas⁸ offers hope that, sooner than later, infant PCV immunization and its attendant benefit on reduction of adult pneumococcal disease will become a reality. Until then, it would appear prudent to offer the benefit of PPV to those at high-risk for invasive pneumococcal disease, with ongoing surveillance to document that pneumococcal serotypes causing IPD from across the country continue to be covered by serotypes in the vaccine.

3. Conclusions

PPV appears beneficial in preventing invasive pneumococcal disease in adults. In the resource-limited setting, PPV may be offered to those at risk of pneumococcal disease while stepping up surveillance to document the burden of disease and to help decide the best possible strategies for introduction of pneumococcal vaccine.

Conflicts of interest

The author has none to declare.

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