



The Importance of Adult Vaccination: Focusing on Pneumococcal Meningitis

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Abstract

The shift of the population to older ages will impact health conditions and quality of life. Older adults are more fragile, with multiple comorbidities and waning immunity. These risk factors will lead to a higher infection rate, mainly if the population lacks herd immunity against vaccine-preventable diseases. Primarily affecting elderly persons, pneumococcal meningitis (PM) is one of the fatal infections that can be prevented by vaccination. Not only does PM affect morbidity and mortality, but it also contributes to a high economic burden. Although the administration of antibiotics and dexamethasone is the mainstay therapy for PM, prevention before contracting the pathogen must be emphasized. Herein, we present pneumococcal vaccination's importance in preventing pneumococcal meningitis in adults.

Keywords: adult vaccination, PCV, pneumococcal meningitis, PPSV.

Introduction

The world population will shift toward older ages. The global population of adults over 60 will rise by 40%, from 1 billion in 2020 to 1.4 billion in 2030.¹ The average lifespan in the world has continued to rise, increasing from 64.2 years in 1990 to 72.6 years in 2019 and is projected to reach 77.1 years in 2050.² By 2050, up to 80% of older people are expected to live in low- and middle-income countries (LMICs).¹ This epidemiological shift will become a challenging situation, especially regarding communicable and non-communicable diseases in sustaining healthy ageing. Adult vaccinations are one of the means to treat this condition. Vaccination will benefit adults who may not have developed immunity and/or who may have waning immunity.³ The implementation of adult vaccination will not only benefit in reducing morbidity, mortality, and hospitalization costs and improving quality of life but more importantly, it will also protect adults from antimicrobial resistance.⁴

Pneumococcal conjugate vaccine (PCV) is a routine childhood immunization worldwide. However, PCV vaccination in adults is not widely recommended; for instance, it is only recommended in 9 out of 16 countries studied in Europe.⁵ A national survey of adult vaccination coverage in the United States in 2021 revealed very low adult (19–64 years) PCV vaccine coverage of 22.2%. The vaccination rate is higher in older adults aged ≥ 65 years (65.8%).⁶ Another study in Canada and Mexico also found relatively low coverage of older adults' PCV vaccination (54.7% and 32–53%), respectively.⁷ Routine PCV immunization will result in protection against pneumococcal diseases, including pneumococcal meningitis.

The prevalence of invasive pneumococcal disease (IPD) in older adults varies through studies. In Sweden, the annual incidence of IPD was 15/100,000; however, in older adults (≥ 65 years), the incidence is three times higher (45/100,000).⁸ In Poland, adults older than 85 years old had a high case fatality rate of IPD (59.7%).⁹ In Italy, there was an increment in IPD incidence, from 0.88/100,000 to 2.82/100,000. Incidence of IPD by age group was 1.8 per 100 000 people between the ages of 25 and 64, and 7.3 per 100 000 people above the age of 64.¹⁰ In Taiwan, the incidence of IPD was primarily found in the older population (aged >65 years; 1147 per 100,000 population). A national health survey in Thailand reported that 26 per 100,000 adults aged ≥ 75 years were diagnosed with IPD.¹¹ In Korea, the incidence of IPD was higher in older adults aged ≥ 65 and those aged 60 to 64 (32.1/100,000 population and 15.7/100,000 population, respectively).¹² The risk of contracting IPD is increased in immunocompromised states such as HIV, autologous or allogeneic stem cell transplantation, solid organ transplantation, and chronic inflammatory diseases.¹³

Besides the incidence, the mortality rates and economic burden of IPD are also very high. There were a total of 2.51 million (2.11–2.99) cases of meningitis, of which *S. pneumoniae* comprised 13.0% (12.4–13.6) of total cases in 2019 with a high mortality rate of 18.1% (95% UI 17.1–19.2) of total all-age meningitis deaths.¹⁴ The mortality of IPD ranged from 14.1% to 22.1% in Asian Studies.^{12,15,16} The case fatality rate of IPD-associated meningitis is 9.6% (7/73; 95% CI: 4.7, 18.5).¹⁶ The average indirect cost per treatment of pneumococcal meningitis in Turkey was \$34,392.25 in the comorbid subpopulation aged 18–64 years and \$17,219.52 in the elderly aged 65–85 years. The sequelae of meningitis also burdened the average indirect cost, with severe disability and persistent vegetative states being the highest ones.¹⁷ A study in Taiwan during 2002–2009 in patients aged ≥ 50 years showed the direct cost per case of pneumococcal meningitis ranging from NT\$ 193,528 to NT\$ 344,621 and the indirect cost per case ranging from NT\$ 4496 to NT\$ 15,960.¹⁸ Pneumococcal meningitis cost Malaysia RM 4,985 for inpatients and RM 515 for outpatients in 2008–2009, with a total direct cost of RM 1,951,773.¹⁹ A systematic review in Latin America and the Caribbean reported up to five times higher costs in the sequelae of pneumococcal meningitis compared to acute pneumococcal meningitis.²⁰

There has been a reported decline in the incidence of IPV after the routine PCV vaccination. In Ontario, Canada, there was a decrease in the incidence of 7-valent PCV and 13-valent PCV (3.0 to 0.7 cases per 100,000 population and 9.8 to 5.3 cases per 100,000 population, respectively).²¹ A study in Catalonia, Spain, reported a declining incidence of IPV in adults aged ≥ 65 years by 35% (22.8 to 14.8) after routine PCV immunization.²² In this review, we aim to assess the importance of adult PCV vaccination for pneumococcal meningitis.

The importance of PCV vaccination for pneumococcal meningitis

Pneumococcal meningitis (PM) is one of the most fatal manifestations of IPD, which has a high case fatality rate of 17.3% (95% CI 15.4%–19.3%) in patients aged 5–64 and 31.9% (219/686; 95% CI 31.8%–39.5%) in patients older than 65.²³ However, following the administration of the PCV vaccination, the incidence of PM declined. Over a 20-year period, a nationwide study conducted in the Netherlands found that the incidence of PM decreased from 1.07 to 0.73 (2007 vs 2017–2018, incidence rate ratio 0.69 (95% CI: 0.56–0.85)) following the introduction of the PCV-7 immunization in June 2006. Concurrently, between 2007 and 2017, non-PCV serotypes rose from 0.45 to 0.68.²⁴ During the sixteen-year surveillance period in England and Wales, the introduction of the PCV-7 vaccination did not change the incidence of

PM (0.60/100,000 person-years to 0.59/100,000 person-years). However, the incidence of PM significantly decreased (0.27/100,000 person-years) following the introduction of PCV-13.²³ During the 2013–2014 study period, there was a substantial monthly decrease in the total PM cases among people over 64 (-2.0; 95% CI, -3.36 to -0.57) following the introduction of PCV7 (2003) and PCV13 (2010) in France.²⁵ In Burkina Faso, the incidence of PM in adults caused by the PCV13 serotype decreased by 64% (95% CI, 53%–72%) after the routine immunization program.²⁶ The results also show a significant reduction in the US after PCV13's introduction in 2010. Between 2008 and 2014, the overall incidence of PM dropped substantially from 0.62 cases per 100,000 (95% CI 0.59, 0.65) to 0.38 cases per 100,000 (95% CI 0.36, 0.40; $P < 0.01$). By age group, the incidence of PM also declined significantly. In the 18-39 year group, the incidence of PM declined from 0.25 cases to 0.15 cases per 100,000; in the 40-64 year group, the incidence of PM declined from 0.95–0.54 cases per 100,000; and in the ≥ 65 age group, PM hospitalizations decreased by 38% (1.02–0.63 cases per 100,000).²⁷ A study in France and Israel also showed a reduced incidence of pneumococcal meningitis caused by vaccine-type pneumococcal.^{28,29}

The vaccination also helps reduce the treatment cost of PM. The benefit of vaccination was \$207.02 in a study in Turkey across the age groups. This will benefit more if vaccination is administered at younger ages.¹⁷ After the introduction of PCV10 and PCV13 in Indonesia, there was a decline in pneumococcal meningitis, with 1,702,548 cases and 2,268,411 cases, respectively. Additionally, vaccinations may save the costs of treatment for PCV10 and PCV13 by \$53.6 million and \$71.4 million, respectively.³⁰ In Northern Ghana, pneumococcal meningitis still has a significant economic effect despite infant vaccination; the cost of treating PCV13-type meningitis in adults (≥ 15 years of age) is \$2,883.³¹ It can be concluded that infant immunization is not enough to provide herd immunity in adults, as there will be waning immunity, especially in older adults. Besides the benefit in reducing morbidity and mortality of pneumococcal diseases, a recent systematic review and meta-analysis reported the benefit of pneumococcal vaccine (PPV23) in reducing the risk of any cardiovascular event, myocardial infarction, and mortality, particularly in older adults (aged ≥ 65 years).³²

Pneumococcal vaccine recommendations

The CDC recommends pneumococcal vaccination based on a previous history of PCV immunization. For older adults (age ≥ 65 years), one dose of PCV15 or PCV20 is recommended for those whose history of vaccination is unknown or who have only received the PCV7 vaccination. If PCV15 is used, it must be boosted by administering PPSV23 at intervals of 1

year. If previously received the PCV13 vaccination, one dose of PCV20 or PPSV23 could be administered with a minimum interval of 1 year after the last PCV13 dose. If the patient has previously received the PPSV23 vaccination, one dose of PCV15 or PCV20 is recommended one year after the previous PPSV23 dose. If previously received PCV13 at any age and PPSV23 at <65 years, one dose of PCV20 or PPSV23 is recommended at least five years after the last pneumococcal vaccination. The interval of PPSV23 administration could be reduced to a minimum of 8 weeks in adults with immunocompromising conditions, cochlear implants, or CSF leaks.³³

In adults (age 19–64 years) with a specified immunocompromising state, the recommendations for pneumococcal vaccination are as follows: 1 dose of PCV15 or PCV20 is recommended for those whose immunization history is unknown or who only received the PCV7 vaccination. If PCV15 is used, one dose of PPSV23 must be administered at an interval of at least eight weeks. If previously received PCV13 vaccination, one dose of PCV20 could be administered with an interval of at least one year after the last PCV13 dose or one dose of PPSV23 could be administered with an interval of at least eight weeks after the previous PCV13 dose, and an additional one dose of PPSV23 could be administered five years after the last PPSV23 dose. If the patient has previously received the PPSV23 vaccination, one dose of PCV15 or PCV20 is recommended one year after the previous PPSV23 dose. If previously received PCV13 and one dose of PPSV23, one dose of PCV20 or PPSV23 is recommended at least five years after the previous pneumococcal vaccination. If previously received PCV13 and two doses of PPSV23, one dose of PCV20 is recommended at least five years after the previous pneumococcal vaccination. Specified immunocompromising states include chronic renal failure, HIV infection, multiple myeloma, congenital or acquired asplenia, Hodgkin disease, nephrotic syndrome, congenital or acquired immunodeficiency, iatrogenic immunosuppression, sickle cell disease/other hemoglobinopathies, leukaemia, generalized malignancy, lymphoma, and solid organ transplant.³³

In adults (age 19_64 years) with a cochlear implant or cerebrospinal fluid leak, the recommendations for pneumococcal vaccination are as follows: 1 dose of PCV15 or PCV20 is recommended for those whose vaccination history is unknown or who only received the PCV7 vaccination. If PCV15 is used, one dose of PPSV23 must be administered at an interval of at least eight weeks. If previously received the PCV13 vaccination, one dose of PCV20 could be administered at a minimum interval of 1 year after the last PCV13 dose, or one dose of PPSV23 could be administered at a minimum interval of 8 weeks after the last PCV13 dose. If the patient has previously received the PPSV23 vaccination, one dose of PCV15 or PCV20 is

recommended one year after the last PPSV23 dose. If previously received PCV13 and one dose of PPSV23, one dose of PCV20 or PPSV23 is recommended at least five years after the last pneumococcal vaccination.³³

In adults (age 19–64 years) with chronic health conditions, the recommendations for pneumococcal vaccination are as follows: 1 dose of PCV15 or PCV20 is recommended for those whose history of vaccination is unknown or who only received the PCV7 vaccination. If PCV15 is used, it must be boosted by administering PPSV23 at intervals of 1 year. If previously received the PCV13 vaccination, one dose of PCV20 or PPSV23 could be administered with a minimum interval of 1 year after the last PCV13 dose. If the patient has previously received the PPSV23 vaccination, one dose of PCV15 or PCV20 is recommended one year after the previous PPSV23 dose. No vaccination is recommended if the patient has previously received PCV13 and PPSV23. Chronic health conditions include alcoholism, chronic lung disease, chronic heart disease, cigarette smoking, chronic liver disease, and diabetes mellitus.³³

In Indonesia, the guideline for adult vaccination is recommended by the Indonesian Society of Internal Medicine. The recommendations for PCV13 are as follows: one dose of PCV13 is recommended for adults >18 years old. If there is no history of PCV vaccination, it is recommended to administer one dose of PPSV23 after PCV13 vaccination with a minimum interval of 8 weeks. If the patient has previously received the PPSV23 vaccination, administer one dose of PCV13 with a minimum interval of 1 year after the last dose of PPSV23. It is highly recommended for patients with chronic health conditions in immunocompromising states and Hajj pilgrims. The PPSV23 (one dose) is recommended for all adults aged ≥ 50 years.³⁴

Conclusion

Our review found several studies regarding the declining incidence and mortality rate of PM in adults after pneumococcal vaccination. The pneumococcal vaccination also alleviates the economic burden of PM by saving treatment costs. These benefits should be marked as one of the means to reduce the overall burden of PM. Healthcare providers should recommend the pneumococcal vaccination to adults at risk (chronic health conditions or immunocompromised states) and older adults, as waning immunity may occur, and they pose a greater threat of contracting the pathogens. The administration of the pneumococcal vaccine should be considered by type of vaccine, patients' age, and existing comorbidities. Government, public health services, and physicians should encourage adults to get vaccinations, as they benefit their overall health and quality of life.

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