

Pneumococcal Vaccines: A Public Health Perspective



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Abstract

The Latin American Thoracic Association (ALAT, for its acronym in Spanish) is working to reinforce vaccination recommendations against pneumococcal disease, a disease that causes multiple consequences, from physical to social and economic, not only in children but also in adults. On November 24th, a forum of experts was held through Zoom platform. Issues such as: Disease burden, implementation recommendations, action steps, and scope of vaccination were discussed.

Keywords: Vaccines; Pneumococcal; Public Health; Pneumococcal Vaccines; COVID-19

Abbreviations: ALAT: Latin American Thoracic Association; GBD: Global Burden of Disease; CAP: Community-Acquired Pneumonia; EPI: Expanded Program on Immunization; WHO: World Health Organization; WHA: World Health Assembly; PPSV23: 23-Component Pneumococcal Polysaccharide Vaccine; ACIP: Advisory Committee on Immunization; CDC: Practices Center for Disease Control and Prevention; PCV13: 13-Component Pneumococcal Conjugate Vaccine; FDA: Food and Drug Administration

Introduction

Streptococcus pneumoniae (pneumococcus) is a Gram-positive, capsulated coccus [1] known to be associated with high morbidity and mortality worldwide, mainly among children and in low-income countries, which have less access to bacterial diagnosis and disease treatment. This pathogen is a major etiologic cause of acute otitis media, pneumonia, meningitis and septicemia, as well as co-infections and superinfections in high-risk groups. Pneumococci colonize the nasopharynx and this carriage precedes disease, being the main source of spread among people, especially in children [2,3]. Colonization is usually asymptomatic, but they can spread to the lower respiratory tract and cause pneumonia or migrate to other body sites where they cause invasive disease such as bacteremia and meningitis [4]; this colonization is dynamic and varies from 30-75% in healthy children (especially those attending day care centers) [5], to 20-30% in healthy adults [6].

Among the pathogens that colonize the respiratory tract, pneumococci cause the most disease, especially when risk factors

are present, making them one of the leading causes of lower respiratory tract infections worldwide [4]. Lower respiratory tract infections and pneumonia are the deadliest communicable diseases worldwide, ranking as the fourth leading cause of death, with more than 4 million deaths per year [7,8]; the 2017 Global Burden of Disease (GBD) study [9], estimated that lower respiratory tract infection caused by influenza accounted for 9,459,000 hospitalizations and 145,000 deaths among all age groups, with the highest mortality rate among adults older than 70 years; meanwhile, for 2016, infection by *S. pneumoniae* was the leading cause of morbidity and mortality from lower respiratory infections worldwide, contributing to 1,189,937 deaths [10].

Pneumococcal Disease

One of the major risk factors for severe pneumococcal disease is preceding viral infections, especially Influenza virus serotype A. Secondary pneumococcal infections occurring during or after a viral infection are usually associated with unfavorable clinical outcomes, whereas a combined influenza and pneumococcal

infection may be a co-infection or a secondary bacterial infection after influenza; in the case of coinfections, these are recognized as an underlying etiology of hospital-acquired pneumonia and community-acquired pneumonia (CAP), the latter being an acute infection that represents a significant burden of disease, especially in those population groups that are most susceptible to developing it: elderly and people with chronic diseases [4].

A prospective study conducted in three South American cities reported that incidence rates of CAP are higher in adults older than 65 years; of the participants included in the study, 82.4% had at least one underlying disease and 48% had two or more [11]. The increased risk of pneumococcal disease associated with established risk factors has persisted in the era of widespread vaccination of children with pneumococcal conjugate vaccines. Rates of pneumococcal disease increased substantially among persons with more than one risk condition, and rates of disease were especially high among people with ≥ 3 risk conditions for younger adults, with a rate of all-cause pneumonia 15.6 times higher than that of healthy persons [12].

Multimorbidity is the coexistence of two or more chronic diseases; comorbidity, the conceptual predecessor of multimorbidity, was originally defined by Feinstein as “any additional distinct clinical entity that has existed or may occur during the course of a patient having the index disease under study” [13]. The prevalence of multimorbidity is over 60% worldwide and is likely to be over 80% among people over 85 years old. The main causes of chronic disease death can be attributed to four major underlying risk factors: smoking, unhealthy eating habits, alcohol consumption and sedentary lifestyle [14], which results in a direct impact on people’s functional status, poor life quality and overall risk of death.

S. Pneumoniae Vaccines

In the last decades, immunization and its related advances have contributed to global development not only scientifically but also socially and economically; six vaccine-preventable diseases were the initial focus of the Expanded Program on Immunization (EPI) more than four decades ago, and at least six new vaccines have increased the breadth of protection provided by immunization. The World Health Organization (WHO) 2030 Agenda for Immunization envisions “a world in which everyone, everywhere and at every age, benefits fully from vaccines to improve health and well-being,” for which it has been developed in a co-creation process with the full country engagement to ensure that the vision, strategic priorities, and goals are aligned with country requirements [15].

Factors supporting the progress achieved with immunization include improvements in health service delivery infrastructure; active surveillance of vaccine-preventable diseases promoted by national, regional and global laboratories; community involvement in vaccination programs and awareness of the vaccine’s social value; data collection, management, analysis and use through

electronic systems; vaccine research and development capacity; and evidence-based policy decision making; data collection, management, analysis and use through electronic systems; vaccine research and development capacity; as well as science-based policy decision-making [15]; additionally, immunization has contributed to Millennium Development Goal 4: Reduce child mortality, according to data from the Inter-agency Group for Child Mortality Estimation (UN-IGME), the under-five mortality rate per 1000 live births decreased from 75.83 in 2000 to 36.63 in 2020 [16].

The worldwide expansion of immunization programs started in 1974 with the establishment of the EPI by the World Health Assembly (WHA) [17], by 1983 a 23-component pneumococcal polysaccharide vaccine (PPSV23) was licensed in the United States, which was subsequently recommended by the Advisory Committee on Immunization Practices (ACIP) of the Center for Disease Control and Prevention (CDC), for all persons aged ≥ 65 years, as well as for those aged ≥ 2 years with chronic diseases associated with an increased risk of pneumococcal infection or complications of pneumococcal infection [3,12]. In 2011, the 13-component pneumococcal conjugate vaccine (PCV13) was licensed in the United States, and the ACIP recommended in 2012 that adults aged ≥ 19 years with immunocompromising conditions, anatomic or functional asplenia, cerebrospinal fluid leaks, or cochlear implants receive PCV 13 followed by PPSV23 [18].

In September 2014, the ACIP reviewed its pneumococcal vaccination recommendation for adults aged 17 years and older to include the use of PCV13 in all adults aged ≥ 65 years, this update boosted the use of PPSV23 with PCV13 in this population [19]; following this recommendation, a group of scientists conducted the first real-world data study, to evaluate the efficacy of PCV13 against hospital-type CAP in this population, using a negative test design, enrolled 2034 patients between cases and controls and concluded that the vaccine effectiveness of PCV13 against CAP in hospitalized population was 73% [20]. The most recent approval was in June 2021 when the US Food and Drug Administration (FDA) approved the 20-element conjugate vaccine for the prevention of invasive disease and pneumonia caused by 20 serotypes of *S. pneumoniae* in adults aged ≥ 18 years [21].

Another study [22] evaluated the efficacy of PCV13 in the prevention of first episodes of nonbacteremic and noninvasive community-acquired pneumonia and invasive pneumococcal disease vaccine strains, demonstrating that, among adults older than 65 years, PCV13 was effective in preventing the mentioned pathologies, maintaining such efficacy for at least four years, but not in preventing CAP due to any cause; being in accordance with other studies that have shown that, although purified capsular polysaccharides are effective against invasive pneumococcal disease in adults, their efficacy against non-invasive pneumonia is uncertain.

In March 2017, WHO held a meeting to identify policies and activities to promote access to vaccination for older adults, specifically in low- and middle-income countries [23], the discussion at the meeting highlighted many reasons and benefits for vaccinating older adults and any age group after childhood; regarding these reasons, they raised three core pillars:

I. Improvement in population immunity (herd) and disease control, by updating the coverage of the complete childhood vaccination schedule when it is not 100%, as well as the application of vaccines not used in adults when they were children (e.g., Measles, Rubella, Mumps, Hepatitis B, Varicella Zoster, Pneumococcal conjugate), and finally, in order to protect against pathogens with new strains or serotypes that may differ by age group (e.g., Influenza and Pneumococcus).

II. Protection of at-risk populations after childhood, this point is aimed at protection against pathogens associated with specific careers or employments, such as health care workers and farm workers with food products or in contact with animals. Also considered under this item is the prevention of hospitalized patient infections and the high morbidity and mortality rate of respiratory diseases in adults.

III. Protection throughout life, with emphasis on the protection of women during and after pregnancy to protect themselves and their babies, as well as vaccination as a primary measure to prevent the unnecessary use of antibiotics and avoiding the increase of antibiotic resistance; also proposed was the vaccination of travelers and vaccination to protect against emerging diseases, outbreaks and pandemics.

Regarding the barriers to adult vaccination in low- and middle-income countries, the experts discussed five central issues:

i. Evidence for action, with loss of burden disease economic data, recommendations in vaccination schedules and public policies issued on the subject.

ii. Individual factors and lack of information about vaccination to the population, leading to vaccine reticence.

iii. Vaccination process with very complex vaccination schedules in adults, with unplanned logistics where people must schedule several visits to obtain the prescription, supplies and then the immunization. Additional prioritization of children's immunization schedules.

iv. Vaccination system with limitations in infrastructure and human resources, lack of technical equipment to support vaccination campaigns, as well as lack of resources for the purchase and distribution of vaccines in adults, urban centralization of vaccination posts and lack of training for health personnel.

v. Community perception of adult health, since, in certain circumstances, society places the elderly's health in an inferior position compared to children's health.

Pneumococcus and COVID-19

The COVID-19 pandemic has highlighted the vulnerability of immunization programs, an essential health service, opening the door for resurgences of vaccine-preventable diseases and further complicating the pandemic situation. In the first quarter of 2020, severe declines in immunization coverage, ranging from 10% to 50% compared to 2019, occurred due to the implementation of severe social and physical distancing policies in many countries around the world [15]. The literature about the safety or efficacy of pneumococcal vaccine in the context of the COVID-19 pandemic is limited; in a cohort study of 11,672 people, 818 of whom had COVID-19, scientists found that people who had been given a pneumococcal vaccine in the same year as the study, had a lower risk of contracting COVID-19 [24], concluding that pneumococcal vaccination reduces the incidence of hospitalizations for pneumonia in adults over 65 years old, which is important because elderly people with COVID-19 infection have the highest risk of mortality [25].

In a retrospective study of 257 patients with laboratory-confirmed COVID-19, bacterial coinfections were observed to be dominant in all patients with COVID-19, with *S. pneumoniae* being the most common pathogen, suggesting that pneumococcal conjugate and polysaccharide vaccines offer an effective approach to prevent the most common coinfection during the COVID-19 pandemic [26]. It is likely that pneumococcal vaccination can mitigate the impact of COVID-19 on healthcare systems by reducing morbidity and mortality due to non-COVID-19 respiratory infections, especially in those with significant risk factors such as advanced age and multimorbidity. It has been estimated that there are 10% of preventable COVID-19 deaths due to pneumococcal superinfection; these deaths could potentially have been prevented with vaccination [24].

Conclusion

The "real world" vision offered by vaccination efficacy data is essential when planning public health initiatives, and in the pneumococcal vaccines case it is essential to analyze the adult population, removing the paradigm that vaccines are only for children, opening it to the fact that non-vaccination in adults represents a significant disease burden and therefore requires their implementation, which combined with the vaccination of minors, becomes a family prevention strategy. Additionally, it should be taken into account that respiratory disease vaccination, particularly against pneumococcus, has a positive impact not only on the population's health, but also on the resources assigned to it.

The COVID-19 pandemic, in its almost 2 years, has demonstrated that vaccines are powerful weapons for the infectious disease control, and that pneumococcal vaccination is fundamental for the control of the pandemic, as it decreases the

burden of pneumonia disease, releasing resources and increasing the capacity for COVID care, in addition to protecting against complications due to pneumococcal co-infection. The pandemic also presents an opportunity for co-administration of vaccines, due to the fact that the risk groups for COVID-19, pneumococcal disease and influenza are similar. Finally, educating the population and raising awareness about the importance of vaccines will be reflected in fewer missed opportunities for vaccination and higher coverage in the target groups.

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