www.jpnim.com Open Access eISSN: 2281-0692
Journal of Pediatric and Neonatal Individualized Medicine 2013;2(2):e020210
doi: 10.7363/020210 Advance publication: 2013 Aug 12

Review

Antipneumococcal vaccination

Gian Vincenzo Zuccotti, Chiara Mameli

Department of Pediatrics, Luigi Sacco Hospital, University of Milan, Milan, Italy

Proceedings

Proceedings of the 9th International Workshop on Neonatology · Cagliari (Italy) · October 23rd-26th, 2013 ·
Learned lessons, changing practice and cutting-edge research

Abstract

Streptococcus pneumoniae (SP) is a gram-positive bacterium with more than 90 known serotypes causing around 11% of all deaths worldwide in children aged 1-59 months. A new era in prevention of SP-related diseases started in at the beginning of 2000s when a 7-valent pneumococcal conjugate vaccine (PCV7) was recommended as the vaccine of choice in pediatric age. PCV7 dramatically reduced invasive pneumococcal diseases (IPD) among children with indirect effects noted among other age groups as well. However, thanks to a strict surveillance network, an increase in non-vaccine serotypes (NVTs) causing IPD was noted worldwide and in late 2000s a new second generation vaccine (13-valent pneumococcal conjugate vaccine-PCV13) with an expanded serotype coverage was licensed. Due to the lack of solid effectiveness data, up to know it is difficult to predict how the composition of NVTs will change after the large-scale introduction of PCV13 or whether the characteristics of the serotypes will change. Long-term surveillance of both IPD, pneumonia, acute otitis media and carriage will be crucial to ascertain whether these second generation vaccines are having the desired effect of reducing the incidence of diseases in the long term.

Keywords

Streptococcus pneumoniae, antipneumococcal vaccination, children, 13-valent pneumococcal conjugate vaccine-PCV13, invasive pneumococcal diseases, *Streptococcus pneumonia* carriage.

Corresponding author

Gian Vincenzo Zuccotti, Department of Pediatrics, Luigi Sacco Hospital, University of Milan, Milan, Italy; email: gianvincenzo.zuccotti@unimi.it.

How to cite

Zuccotti GV, Mameli C. Antipneumococcal vaccination. J Pediatr Neonat Individual Med. 2013;2(2):e020210. doi: 10.7363/020210.

Vaccination is widely considered one of the greatest achievements of modern era. The golden age of vaccinology started after World War II, when new vaccines were developed and become available in a relatively short period. Their success was proved by the control of life-threatening diseases such as those caused by *Haemofilus influenzae*, poliovirus, *Corynebacterium diphtheria*, *Clostridium tetani* and by the reduction of the incidence of diseases with significant morbidity as measles, rubella and hepatitis B after mass vaccination. Besides the improvement of infectious disease control, surveillance networks have made, and continue to make, significant progress over the past years. Lesson learned from epidemiological studies showed that the acquisition of new vaccine should be considered a starting point in the control of infectious diseases and the best example in this field was provided by *Streptococcus pneumoniae* vaccination.

Streptococcus pneumoniae is a gram-positive bacterium with more than 90 known serotypes causing around 11% (8-12%) of all deaths worldwide in children aged 1-59 months (excluding pneumococcal deaths in HIV-positive children) [1]. *Streptococcus pneumoniae* is carried in nasopharynx and is spread by airborne droplets within the community [2]. Highest frequency of pneumococcal colonization are found in children under the age of 5, thus this risk group is thought to be the most important vector for horizontal dissemination of pneumococcal strains within the community. *Streptococcus pneumoniae* colonization has been considered the key to pneumococcal disease and usually precedes both invasive diseases (IPD) such as bacteremia, meningitis, and bacteriemic pneumonia and acute otitis media (AOM), the most common clinical manifestation of pneumococcal infection among children and the most common outpatient diagnosis resulting in antibiotic prescriptions in that group [3].

A new era of prevention of *Streptococcus pneumoniae*-related diseases started in 2000s when a 7-valent pneumococcal conjugate vaccine (PCV7), licensed by the Food and Drug Administration (FDA) for use among infants and young children, was recommended as the vaccine of choice in pediatric age [4]. The immunization with polysaccharides conjugated to a carrier protein resulted in induction of protective levels of antibodies also in children under 2 years of age as well as immunological memory and contributes to reduce the nasopharyngeal carriage of this pathogen. Approved in more than 70 countries, PCV7 dramatically reduced IPD among children younger than 2 years, with indirect effects noted among other age groups as well within 1 year of routine use [5]. Data available worldwide demonstrates that vaccine-serotype IPD declined by 90% among the age group recommended for vaccination, and indirect effects have been documented in unvaccinated age group as older infants and elderly [6-9]. Additionally, declines in other pneumococcal diseases such as AOM have been reported, highlighting the extended benefits of this vaccine [9-10].

The epidemiological effect of such a broad-scale use of PCV7 was difficult to determine *a priori*, and the capillary surveillance all over the word was essential and determinant to assess the effects of mass vaccination in each region where PCV7 was introduced [11]. Thanks to the effort of surveillance networks the scientific community realized that the pneumococcal population has changed since the widespread introduction of PCV7. Non-vaccine serotypes (NVTs) have increased among carriers and as causes of IPD, particularly 19A [12-14]. This phenomena named "serotype replacement" has showed that vaccines can put new evolutionary pressures on circulating strains, favoring those that are most resistant to the neutralizing activity of vaccination-induced immunity. This changed epidemiologic scenario forced the scientific community to think about new effective vaccination strategy in order to expand the serotype vaccine coverage and, as consequence, second generation vaccines were licensed. On 2010 a new 13-valent pneumococcal polysaccharide-protein conjugate vaccine (PCV13) was approved by FDA for prevention of IPD caused among infants and young children by the 13 serotypes in the vaccine [15-16]. PCV13 contains the seven serotypes included in PCV7 (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) and six additional serotypes (1, 3, 5, 6A, 7F, and 19A) that emerged as major causes of IPD in post-PCV7 era. Also a 10-valent pneumococcal polysaccharide-protein conjugate vaccine (PCV10) was licensed at the end of 2000s [17].

To date few data are available about the real impact of PCV13 on *Streptococcus pneumoniae*-related diseases and carriage. Singleton et al. showed that PCV13-serotype IPD incidence declined significantly after PCV13 introduction. They concluded that although non-PCV13-serotype IPD also declined significantly, absence of PCV13-serotype IPD in children who received PCV13 suggests a protective vaccine effect [18]. A study in

young children (< 2 years) children suggested that PCV13 has an impact on overall carriage, as well as on serotypes 19A, 7F, and 6C [19].

Due to the lack of solid effectiveness data, up to know it is difficult to predict how the composition of NVTs will change after the large-scale introduction of PCV13 or whether the characteristics of the serotypes will change. Strategic Advisory Group of Experts (SAGE) recently recommended that post-PCV introduction surveillance should be undertaken for at least 5 years and be paired with at least 2 years of high quality, pre-vaccine introduction disease surveillance in order to clearly understand the biologic impact of PCV-13 on pneumococcal diseases [20]. Long-term surveillance of both IPD, pneumonia, AOM and carriage will be crucial to ascertain whether these second generation vaccines are having the desired effect of reducing the incidence of disease in the long term. Epidemiological data will tell us if new vaccines candidates will need to be developed and if the scientific community should start to think to a third era in *Streptococcus pneumoniae*-related disease prevention.

Declaration of interest

None of the Authors had any conflict of interest.

References

1. O'Brien KL, Wolfson LJ, Watt JP, Henkle E, Deloria-Knoll M, McCall N, Lee E, Mulholland K, Levine OS, Cherian T; Hib and Pneumococcal Global Burden of Disease Study Team. Burden of disease caused by Streptococcus pneumoniae in children younger than 5 years: global estimates. Lancet. 2009;374(9693):893-902.
2. http://www.cdc.gov/vaccines/pubs/surv-manual/chpt11-pneumo.html, last access: June 2013.
3. Bogaert D, De Groot R, Hermans PW. Streptococcus pneumoniae colonisation: the key to pneumococcal disease.Lancet Infect Dis. 2004;4(3):144-54.
4. CDC. Preventing pneumococcal disease among infants and young children: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 2000;49(No. RR-9): 1-38.
5. Center KJ. Prevenar vaccination: review of the global data, 2006. Vaccine. 2007;25(16):3085-9.
6. Kaplan SL, Mason EO Jr, Wald ER, Schutze GE, Bradley JS, Tan TQ, Hoffman JA, Givner LB, Yogev R, Barson WJ. Decrease of invasive pneumococcal infections in children among 8 children's hospitals in the United States after the introduction of the 7-valent pneumococcal conjugate vaccine. Pediatrics. 2004;113(3):443-9.
7. Ben-Shimol S, Greenberg D, Givon-Lavi N, Elias N, Glikman D, Rubinstein U, Dagan R; Israeli Bacteremia and Meningitis Active Surveillance Group. Rapid reduction in invasive pneumococcal disease after introduction of PCV7 into the National Immunization Plan in Israel. Vaccine. 2012;30(46):6600-7.
8. Olarte L, Ampofo K, Stockmann C, Mason EO, Daly JA, Pavia AT, Byington CL. Invasive Pneumococcal Disease in Infants Younger Than 90 Days Before and After Introduction of PCV7. Pediatrics. 2013;132(1):e17-24.
9. Myint TT, Madhava H, Balmer P, Christopoulou D, Attal S, Menegas D, Sprenger R, Bonnet E. The impact of 7-valent pneumococcal conjugate vaccine on invasive pneumococcal disease: a literature review. Adv Ther. 2013;30(2):127-51.
10. Ansaldi F, Sticchi L, Durando P, Carloni R, Oreste P, Vercelli M, Crovari P, Icardi G. Decline in pneumonia and acute otitis media after the introduction of childhood pneumococcal vaccination in Liguria, Italy. J Int Med Res. 2008;36(6):1255-60.
11. Weinberger DM, Malley R, Lipsitch M. Serotype replacement in disease after pneumococcal vaccination. Lancet. 2011;378(9807):1962-73.
12. Kaplan SL, Barson WJ, Lin PL, Stovall SH, Bradley JS, Tan TQ, Hoffman JA, Givner LB, Mason EO Jr. Serotype 19A Is the most common serotype causing invasive pneumococcal infections in children. Pediatrics. 2010;125(3):429-36.
13. Pilishvili T, Lexau C, Farley MM, Hadler J, Harrison LH, Bennett NM, Reingold A, Thomas A, Schaffner W, Craig AS, Smith PJ, Beall BW, Whitney CG, Moore MR; Active Bacterial Core Surveillance/Emerging Infections Program Network. Sustained reductions in invasive pneumococcal disease in the era of conjugate vaccine. J Infect Dis. 2010;201(1):32-41.
14. Davis S, Deloria-Knoll M, Kassa HT, O'Brien KL. Impact of pneumococcal conjugate vaccines on nasopharyngeal invasive disease among unvaccinated people: Review of evidence on indirect effects. Vaccine. 2013 May 16. pii: S0264-410X(13)00561-6. doi: 10.1016/j.vaccine.2013.05.005. [Epub ahead of print].
15. Food and Drug Administration. Product approval information – licensing action, package insert: Prevnar 13 (pneumococcal 13-valent conjugate vaccine), Pfizer. Rockville, MD: US Department of Health and Human Services, Food and Drug Administration; 2010. http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm201667.htm, last access: June 2013.
16. CDC. Licensure of a 13-valent pneumococcal conjugate vaccine (PCV13) and recommendations for use among children – Advisory Committee on Immunization Practices (ACIP), 2010. MMWR. 2010;59:258-61.
17. Prymula R, Schuerman L. 10-valent pneumococcal nontypeable Haemophilus influenzae PD conjugate vaccine: Synflorix. Expert Rev Vaccines. 2009;8(11):1479-500.
18. Singleton R, Wenger J, Klejka JA, Bulkow LR, Thompson A, Sarkozy D, Emini EA, Gruber WC, Scott DA. The 13-valent pneumococcal conjugate vaccine for invasive pneumococcal

disease in Alaska native children: results of a clinical trial. Pediatr Infect Dis J. 2013;32(3):257-63.

19. Cohen R, Levy C, Bingen E, Koskas M, Nave I, Varon E. Impact of 13-valent pneumococcal conjugate vaccine on pneumococcal nasopharyngeal carriage in children with acute otitis media. Pediatr Infect Dis J. 2012;31(3):297-301.
20. WHO. Pneumococcal vaccines WHO position paper – 2012. Wkly Epidemiol Rec. 2012;87:129-44.