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Pneumococcal vaccines and pneumonias

Dear Editor,

We have assessed the article "Pneumonia mortality in Brazilian children aged 4 years and younger," by Rodrigues et al.,[1] and found it to be good and interesting data. Nevertheless, we believe a few observations are in order.

One of the major objectives of pneumococcal vaccination is the prevention of community-acquired pneumonia (CAP). Pneumococcal vaccines afford protection against most serotypes associated with CAP.[2,3]

Some studies have reported efficacy against CAP and reduction of hospital admission rates. However, randomized controlled trials are always fraught with difficulty regarding the definition of pneumonia.

The first study to assess effectiveness against pneumonia was conducted in the U.S. state of California, and included 37,868 children who were randomly allocated to receive the heptavalent pneumococcal vaccine or the meningococcal vaccine.[4] Efficacy was 4.3% against clinically diagnosed pneumonia and 20.5%[5] for radiologically confirmed pneumonia using the World Health Organization criteria for standardized interpretation of chest radiographs.

A recent study (the Clinical Otitis Media & Pneumonia Study, COMPAS) comparing 11,875 children who received the 10-valent pneumococcal vaccine versus 11,863 controls reached similar conclusions.[6] Vaccine efficacy was 7.5% for prevention of any pneumonia, 10.5% for prevention of pneumonia with consolidation, 18.2% against pneumonia with consolidation or C-reactive protein >40 mcg/ml, and 23.4% against consolidated pneumonia confirmed by the World Health Organization criteria.[5] Therefore, the more specific the definition of pneumonia, the higher the rate of vaccine efficacy.

The COMPAS study is most recent study and used the same vaccine included in the Brazilian immunizations schedule, and once again showed that vaccine efficacy increases with more specific definitions of pneumonia.[6]

Studies of vaccine efficacy against pneumonias[6-8] are described in Table 1.

After the inclusion of the pneumococcal vaccine in the U.S. immunizations schedule, Grijalva et al.[9] detected a 36.9% decline in all-cause pneumonia admissions and a 64.9% reduction in admissions due to pneumococcal pneumonia.

Rodrigues et al.[1] report a reduction in pneumonia mortality with the diagnosis of pneumonia based on ICD-9 classification—hence, with a clinical, clinician-defined diagnosis. However, there is no mention of the ICD codes used to define pneumonia in the study (apparently, unqualified "pneumonia" was used). Furthermore, the study detected a reduction in pneumonia mortality before the pneumococcal vaccine was added to the Brazilian immunization schedule. This reduction differed across the various regions of the country.[1] The pneumococcal vaccine was introduced to Brazil in March 2010; therefore, the reduction in pneumonia mortality over the study period (1991 to 2007) cannot be ascribed to this vaccine. Even though the vaccine was available from private healthcare providers, the number of immunized individuals would have been insufficient to bring about any detectable changes.

Table 1 - Studies of pneumococcal conjugate vaccine efficacy against community-acquired pneumonia

Location	Vaccine	No. of patients	Efficacy against radiologically confirmed pneumonia	Cases prevented per 1000 vaccinated
Soweto (South Africa) Klugman et al.[7]	PCV-9*	40,000	25% (HIV-negative) 13% (HIV-positive)	2.9
The Gambia Cutts et al.[8]	PCV-9*	17,400	37%	14.2
Argentina, Colombia and Panama Tregnagui et al.[6]	PCV-10 Synflorix (GSK)**	24,000	23%	5.0

* PCV-9: Wyeth -9 pneumococcal vaccine conjugated to the CRM_{197} mutant diphtheria toxoid. PCV-9 contains the seven serotypes present in the heptavalent vaccine (4, 6B, 9C, 14, 18C, 19F, 23F) plus serotypes 1 and 5.

** PCV-10 Synflorix (GSK): pneumococcal vaccine conjugated to non-typeable *Haemophilus influenzae*-derived protein D. Contains the 9 serotypes present in PCV-9, plus serotype 7F.

However, this reduction in mortality can be interpreted as the result of a population-wide improvement in socioeconomic status. Such improvement may be a factor in reductions in pneumonia that precede the availability of vaccines.

A similar scenario occurred prior to introduction of rotavirus vaccine: a reduction in the number of cases of diarrheal disease preceded the start of immunizations.[10] Furthermore, reductions in diarrhea mortality differed across different regions, with the greatest reductions occurring in the poorest areas of the country.[11] Therefore, population-wide improvements in economic status may be followed by decreased incidence of conditions such as pneumonia and diarrheal diseases. As progress does not occur equally in different regions, vaccines will lead to greater reductions in disease such as pneumonia and diarrhea in the most underprivileged areas. Table 1 shows that the greatest protection against pneumonia – 14 cases prevented per 1000 vaccinated – was achieved in an extremely poor country, namely The Gambia.

The introduction of vaccines is always cost-effective, as it will lead to a decline in disease. However, the introduction of novel vaccines requires greater economic progress, as it is a costly (though cost-effective) action.

The immunization success data published in the literature are often from first-world countries such as the U.S., where the introduction of novel vaccines coincides with technological innovation. In Brazil, the introduction of new vaccines is occurring concomitantly with a series of significant improvements in social conditions. An assessment of the epidemiology of pneumonias after pneumococcal vaccine coverage has been extended to the entire population should prove highly relevant.

References

1. Rodrigues FE, Tatto RB, Vauchinski L, Leães LM, Rodrigues MM, Rodrigues VB, et al. Pneumonia mortality in Brazilian children aged 4 years and younger. J Pediatr (Rio J). 2011;87:111-4.
2. Bricks LF, Berezin E. Impact of pneumococcal conjugate vaccine on the prevention of invasive pneumococcal diseases. J Pediatr (Rio J). 2006;82:S67-74.
3. Berezin EN, Cardenuto MD, Ferreira LL, Otsuka M, Guerra ML, Brandileone MC. Distribution of Streptococcus pneumoniae serotypes in nasopharyngeal carriage and in invasive pneumococcal disease in Sao Paulo, Brazil. Pediatr Infect Dis J. 2007;26:643-5.
4. Hansen J, Black S, Shinefield H, Cherian T, Benson J, Fireman B, et al. Effectiveness of heptavalent pneumococcal conjugate vaccine in children younger than 5 years of age for prevention of pneumonia: updated analysis using World Health Organization standardized interpretation of chest radiographs. Pediatr Infect Dis J. 2006;25:779-81.
5. World Health Organization. Pneumonia Vaccine Trial Investigators' Group. Standardization of interpretation of chest radiographs for the diagnosis of pneumonia in children. Geneva: World Health Organization; 2001. WHO document WHO/V&B/01.35.
6. Tregnaghi MW, Sáez-Llorens X, López P, Abate H, Smith E, Pósleman A, et al. Evaluating the efficacy of 10-valent pneumococcal non-typeable Haemophilus influenzae protein-D conjugate vaccine (PHiD-CV) against community-acquired pneumonia in Latin America. 29th Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID). The Hague, The Netherlands; 7-11 June 2011. Abstract 1411.
7. Klugman KP, Madhi SA, Huebner RE, Kohberger R, Mbelle N, Pierce N, et al. A trial of a 9-valent pneumococcal conjugate vaccine in children with and those without HIV infection. N Engl J Med. 2003;349:1341-8.
8. Cutts FT, Zaman SM, Enwere G, Jaffar S, Levine OS, Okoko JB, et al. Efficacy of nine-valent pneumococcal conjugate vaccine against pneumonia and invasive pneumococcal disease in The Gambia: randomised, double-blind, placebo-controlled trial. Lancet. 2005;365:1139-46.
9. Grijalva CG, Nuorti JP, Arbogast PG, Martin SW, Edwards KM, Griffin MR. Decline in pneumonia admissions after routine childhood immunisation with pneumococcal conjugate vaccine in the USA: a time-series analysis. Lancet. 2007;369:1179-86.
10. Gurgel RQ, Ilozue C, Correia JB, Centenari C, Oliveira SM, Cuevas LE. Impact of rotavirus vaccination on diarrhoea mortality and hospital admissions in Brazil. Trop Med Int Health. 2011;16:1180-4.
11. do Carmo GM, Yen C, Cortes J, Siqueira AA, de Oliveira WK, Cortez-Escalante JJ, et al. Decline in diarrhea mortality and admissions after routine childhood rotavirus immunization in Brazil: a time-series analysis. PLoS Med. 2011;8:e1001024

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