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., 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.

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. Efficacy was 4.3% against clinically diagnosed pneumonia and 20.5% 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. 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. Therefore, the more specific the definition of pneumonia, the higher the rate of vaccine efficacy.

The COMPAS study is the 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.

Studies of vaccine efficacy against pneumonias are described in Table 1.

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

Rodrigues et al. 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. 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

<table>
<thead>
<tr>
<th>Location</th>
<th>Vaccine</th>
<th>No. of patients</th>
<th>Efficacy against radiologically confirmed pneumonia</th>
<th>Cases prevented per 1000 vaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soweto (South Africa)</td>
<td>PCV-9*</td>
<td>40,000</td>
<td>25% (HIV-negative) 13% (HIV-positive)</td>
<td>2.9</td>
</tr>
<tr>
<td>Klugman et al.</td>
<td></td>
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<tr>
<td>The Gambia</td>
<td>PCV-9*</td>
<td>17,400</td>
<td>37%</td>
<td>14.2</td>
</tr>
<tr>
<td>Cutts et al.</td>
<td></td>
<td></td>
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<tr>
<td>Argentina, Colombia and Panama</td>
<td>PCV-10 Synflorix (GSK)**</td>
<td>24,000</td>
<td>23%</td>
<td>5.0</td>
</tr>
</tbody>
</table>

* PCV-9: Wyeth -9 pneumococcal vaccine conjugated to the CRM197 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. Furthermore, reductions in diarrhea mortality differed across different regions, with the greatest reductions occurring in the poorest areas of the country. 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

Eitan Naaman Berezin
Doutor. Professor adjunto, Departamento de Pediatria, Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, SP, Brazil. Chefe do serviço de Infectologia Pediátrica, Santa Casa de São Paulo, São Paulo, SP, Brazil. Presidente, Departamento de Infectologia Pediátrica, Sociedade Brasileira de Pediatria.

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