Evolution of Paediatric Invasive Pneumococcal Disease (IPD) after Implementation of a Routine Infant 13-valent Pneumococcal Conjugate Vaccination Program

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Abstract

Background: PCV7 vaccination has resulted in dramatic declines in IPD due to strains included in PCV7, but some increase in IPD due to non-vaccine serotypes (NVT) has occurred. The effectiveness of 10- and 13-valent PCV programs and their impact on IPD due to NVT disease is as of yet unknown.

Methods: In Ontario, PCV7 was authorized in 2001. Publicly-funded PCV7 vaccination was introduced in 1/2005, PCV10 in 10/2009 and PCV13 in 11/2010. The PCV13 program included a catch-up dose for children aged 10-36 months who had not previously received PCV13. TIBDN has performed population-based surveillance for IPD in metropolitan Toronto/Peel region since 1995. All cases of IPD are reported to a central study office. Isolates are shipped to a central study lab for serotyping. Demographic and clinical data are collected by chart review and patient/physician interview.

Results: From 2001-2012 (as of September 30, 2012), 900 cases of paediatric IPD (<15y) have been identified. 557 (56.3%) patients were male and 343 (36.6%) had a chronic underlying illness predisposing them to IPD. The most common diagnoses were pneumonia (353, 35.2%), bacteremia without focus (239, 23.6%), and meningitis (56, 10%). 87 (9.6%) required ICU admission; the 30-day case fatality rate was 1.7% (19/906). IPD incidence was stable from 1995 to 2002. Incidence since 2001 is shown by serotype (ST) category for children aged 6-35 months in Figure 1 and children 0-5 months and 36-48 months in Figure 2. In 2011/12, 68/343 (20%) PCV13 ST cases occurred in vaccine ineligible children, compared to 53/251(21%) in 2009/10 (p<.05). Since the implementation of PCV13, 97 cases of IPD have occurred; 93 were serotyped. ST vaccine data are available for 89. 40 were NVT disease; 34 occurred in children not eligible for PCV13; 2 in children who had not received any PCV; 10 (all PCV13/not PCV10 STs) in children eligible for a catch-up dose of PCV13 who had not received it. Four children (3 ST 19A, 1 ST 18C; 1 with chronic illness) had received PCV13; 2 or 3 doses of PCV13 at age< 7 months; 1 child with cardiac disease (ST19A) had received a single dose of PCV13 at 14 months.

Conclusions: One year after PCV13 implementation, 88% of PCV13 ST disease occurred in children not eligible for PCV13 or eligible but unvaccinated. Although a few cases of PCV13 disease occurred in partially-immunized children, there is evidence that the rate of PCV13/ST10 disease is decreasing in vaccine eligible children.

Methods

From 1995 to 2012, prospective, population-based surveillance for invasive pneumococcal disease (defined as illness associated with a sterile site isolate of a pneumococcal) was conducted in metropolitan Toronto and Peel region (population 4.1 million in 2011).

Serotype is determined using latex pneumococcal antisera (Statens Serum Institute, DK) and the Quellung reaction. Population data was obtained from Statistics Canada. Demographic and clinical data are collected from review of health records and interviews with patients and attending physicians.

PCV programs in Ontario

In Ontario, PCV7 was licensed in June 2001 and, in January 2002, the Canadian National Advisory Committee on Immunization (NACI) recommended routine vaccination of all children aged <24 months. By late 2002, uptake in the private market resulted in usage of approximately 1 dose per child in the birth cohort in Ontario. Data on the distribution of these doses is not available. In January 2005, PCV7 became publicly funded for healthy children. PCV10 was introduced in October 2009 and PCV13 in late November 2010 (Table 1).

Table 1: Licensing and public funding of pneumococcal conjugate vaccines for healthy children, Ontario.

<table>
<thead>
<tr>
<th>Date Vaccin</th>
<th>Availability/program change</th>
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<tbody>
<tr>
<td>Jan 2001 PCV7 licensed</td>
<td>(available private market)</td>
</tr>
<tr>
<td>Jan 2005 PCV7</td>
<td>Public funding for routine immunization (2,4,6,15 months)</td>
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<tr>
<td>Dec 2008 PCV7 licensed</td>
<td></td>
</tr>
<tr>
<td>Nov 2009 PCV10 replaced PCV7 in publicly funded program</td>
<td>Children who have had 1 dose of PCV7 to complete course with PCV7</td>
</tr>
<tr>
<td>Dec 2009 PCV10 licensed</td>
<td></td>
</tr>
<tr>
<td>Nov 2010 PCV13 replaced PCV10 in publicly funded program</td>
<td>Children who have had 2 or 3 doses of PCV13 at age&lt;7 months; 1 child with cardiac disease (ST19A) had received a single dose of PCV13 at 14 months.</td>
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Results

We assessed changes in IPD rates among children aged 6-35 months as compared to children of other ages. If uptake of the November 2010 PCV10 program was complete by January 2011, children aged 6-35 months during 2011-2012 should have been protected from PCV13 serotype IPD, with the exception that children aged 4-9 months of age November 2010 would have received no or only 1 dose of PCV13 before they were 12 months old (between January and June 2011). Similarly, children aged <6 months or >36 months would not be expected to be protected, with the exception that children aged >35 months in November 2010 would have been eligible for a catch-up dose of PCV13.

Between 2001 and 2006, the overall annual IPD incidence decreased among children aged 6-35 months from 53.6 to 12.7 cases per 100,000 population (p<0.001) (Figure 1). In this age group, IPD rates increased in 2009 to 29.9 cases per 100,000 population then decreased to 11.9 cases per 100,000 in 2011 (p<0.004, 2011 vs. 2009). However, in children 0-5 months and 36-48 months (Figure 2), overall IPD incidence decreased from 6.4 cases per 100,000 population in 2001 to 2.7 cases per 100,000 in 2006 (p<0.003), then increased to 4.6 cases per 100,000 in 2011 (p<0.006, 2011 vs. 2006).

Between 2001 and 2011, the reduction of IPD caused by serotypes included in the PCV7 vaccine was significant among children of all ages (Figures 1-2). Changes in rates of IPD caused by PCV13/not PCV7, and non-vaccine serotypes (NVT) differed among vaccinated and non-vaccinated children (Figures 3-4).

Conclusions

The implementation of a routine infant PCV13 vaccination program has been associated with a significant reduction in disease due to PCV13/nonPCV13 ST disease in vaccine-eligible children.

In the first two years after implementation of a routine infant PCV13 vaccination program, no IPD cases occurred in completely immunized children, and only three cases occurred in vaccine eligible children who had received age-appropriate vaccination (3 in children age <12 months who had received 2 or 3 doses of PCV13).

Two or three doses of PCV13 at age<12 months, or 1 dose at age <12 months provided incomplete protection against IPD. Our data do not allow assessment of the degree of protection that may be provided.

Rates of disease due to non-PCV IPD have not increased since 2008.

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