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 disease due to NVT disease is as of yet unknown.

Methods: In Ontario, PCV7 was authorized in 2001. Publicly-funded PCV7 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 12-36m 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, clinical and vaccine 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. 507 (56.3%) patients were male and 139 (15.8%) had a chronic underlying illness predisposing them to IPD. The most common diagnoses were pneumonia (353, 39.2%), bacteraemia without focus (329, 36.6%), and meningitis (90, 10%). 87 (9.6%) required ICU admission; the 30-day case fatality rate was 1.7% (15/900). IPD incidence was stable from 1995 to 2002. Incidence since 2001 is shown by serotype (ST) category for children aged 6-35 mos in Figure 1 and children 0-5 months and 36mos-14yrs in Figure 2. In 2011/12, 68% (34/53) of PCV13 ST cases occurred in vaccine ineligible children, compared to 50% (53/106) in 2008/9 (P=.05). Since the implementation of PCV13, 97 cases of IPD have occurred; 93 were serotyped. ST and 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/not10 STs) in children eligible for a catch-up dose of PCV13 who had not received it. Four children (3 ST 19A, 1 ST18C; 1 with chronic illness) had received 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.

Figure 1: IPD incidence by serotype category among children 6-35 months old , 2001-2011

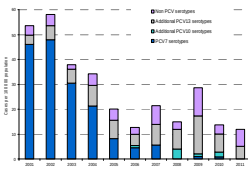
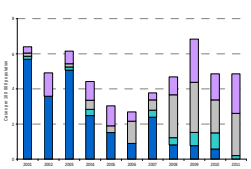


Figure 2: IPD incidence by serotype category in children 0-6months and 3-14 years old, 2001-2011



Conclusion: One year after PCV13 implementation, 89% of PCV13 ST disease occurred in children either 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/not10 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 *S. pneumoniae*) 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.

Date	Vaccine	Availability/program change
Jun 2001	PCV7	Licensed (available private market)
Jan 2005	PCV7	Public funding for routine immunization (2,4,6,15 months)
Dec 2008	PCV10	Licensed
Nov 2009	PCV10	Replaces PCV7 in publicly funded program Children who have had ≥1 dose of PCV7 to complete course with PCV7
Dec 2009	PCV13	Licensed
Nov 2010	PCV13	Replaces PCV10 in publicly funded program Change to 3 dose (2,4,12 months) Catch-up PCV13 dose for children 12-36 months who have completed PCV7 schedule

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 PCV13 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<.0001) (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) (Figure 1). In children 0-5 months and 36mos-14yrs of age (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=0.06, 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 PCV 13/not PCV7, and non-vaccine serotypes (NVT) differed among vaccinated and non-vaccinated children (Figures 3-4).

Results (cont'd)

The six-month rate (Jan-June) of IPD due to PCV13/notPCV7 serotypes in children aged 6-35 months increased from a mean 2.7 cases per 100,000 in 2006/2007 to a mean of 7.1 per 100,000 in 2008/2009 (p=0.03), then decreased to an average 2.5 per 100,000 in 2011/2012 (p=0.04) (Figure 3a).

Rates of PCV13/not PCV7 in children 0-5 months and 3-14 yrs (Figure 3b) increased from 0.5 cases per 100,000 in 2006/7 to 1.5 cases per 100,000 in 2008/9 (p=0.05) and then remained stable through 2011/2012.

Figure 3: IPD due to PCV13 not PCV7 serotypes, by 6 month period, Jan 2006 to July 2012

Figure 3a: Children 6 – 35 mo

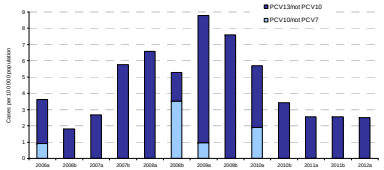
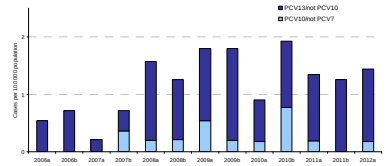


Figure 3b: Children 0-5 mo and 3-14 yrs



The rate of IPD due to non-PCV serotypes in children aged 6-35 months did not change significantly between 2006 and 2012; the average six-month incidence was 2.5, 3.6. and 3.1 cases per 100,000 in time periods 2006/2007, 2008/2009, and 2011/2012, respectively (Figure 4a). In children 0-5 months and 3-14 yrs, non-PCV IPD more than doubled between 2006/2007 and 2008/2009 from a mean of 0.2. to 0.9 cases per 100,000 (p=0.01); there were no changes between 2008/2009 and 2011/2012 (Figure 4b).

Figure 4: IPD due to non vaccine serotypes, by 6 month period, Jan 2006 to July 2012

Figure 4a: Children 6 – 35 mo

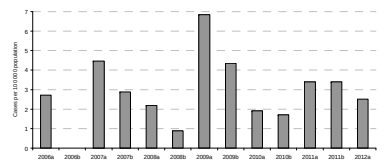
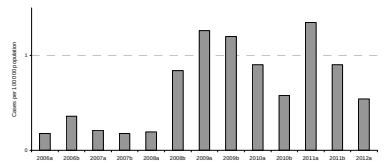


Figure 4b: Children 0-5 mo and 3-14 yrs



Results (cont'd)

During 2011-2012 (to September 30, 2012), 97 cases of paediatric IPD were identified in our surveillance area. Serotyping is available for 93 of the 97, and complete vaccination history for 89 cases. 53 cases were caused by serotypes included in PCV13. 40 were NVT. Characteristics of IPD cases due to PCV13 serotypes are presented in Table 2. Among children 6-35 mo old with known vaccination history, all 13 cases due to PCV13 STs occurred among those who had not completed full course of PCV13) (Table 2). Among children >=36 mo old, 4 children missed catch up PCV13 vaccination (Table 2).

Table 2: Characteristics of 53 paediatric IPD cases identified in 2011-2012 (as of September 30, 2012) caused by serotypes included in PCV13.

Classification	N, cases	Age in months* (range)	Vaccination history	Serotype (N)
Children 6 – 35 mos	15			
Unvaccinated	2	17, 32	No dose of any PCV	19A (2)
Incomplete PCV13 vaccination				
Age <12 months	3	9, 10, 10	Received 2 doses of PCV13 at 2 and 4 mos (n=1), or 3 doses at 2,4 and 6 mos (n=2)	18C , 19A (2)
Age >12 months	2	16, 21	Received 3 doses of PCV13 at 2, 4 and 6 mos (n=1), or received 1 dose of PCV13 at 14 mos (n=1)	19A (2)
Missed catch-up PCV13	6	14 -34	PCV7 at 2, 4, and 6 mos, missed 12 mos PCV7 (n=4); PCV7 at 2,4, 6 and 13/15 mos (n=2)	19A (4), 3 (2)
Unknown vaccination history	2	21,35	N/A	7F (1), 19A (1)
Children 0-5 mos and 3- 14 yrs	38			
Unvaccinated				
Age >=36 mo	5	36-167	No doses of any PCV	19A (4), 9V (1)
Age <2 mo	2	0-2	Too young for vaccination	3 (2)
Missed catch-up PCV13	4	41-44	Received 3-4 doses of PCV7 , age 36 mos Nov/Dec 2010 (eligible for PCV13 catch up)	19A (4)
Complete PCV7 vaccination , not eligible for PCV13 catch-up	18	49-126	Complete course of PCV7 (4 doses) , age >36 month in Nov/Dec 2010	19A(11), 3(2), 7F (5)
Incomplete PCV7 vaccination	4	50-85	Received 2-3 doses of PCV7	19A (3), 3 (1)
Unknown vaccination history	5	49-129	N/A	19A (2), 7F(1), 6B (1)

*Age at time of diagnosis of IPD

Conclusions

➢The implementation of a routine infant PCV13 vaccination program has been associated with a significant reduction in disease due to PCV13/not7 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 (all 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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