The Risk of Febrile Seizures Following Influenza and 13-Valent Pneumococcal Conjugate Vaccines

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Jorge Arana, MD, MPH; Pedro Moro, MD, MPH; Paige Lewis, MSPh; and Maria Cano, MD, MPH.

Introduction. The 13-valent pneumococcal conjugate vaccine (PCV13) was licensed in the United States in 2010 for children 6 weeks–59 months old. The Food and Drug Administration (FDA) licensed the vaccine under the Post-licensure Surveillance System, which monitors adverse event reports (AEs). This study describes the surveillance of PCV13-related AEs from 2010 to 2017.

Methods. VAERS is a passive surveillance system, and reports of adverse events (AEs) following PCV13 from February 24, 2010 through February 24, 2017, were extracted. AEs with onset within 30 days of vaccination were included. AE reports were stratified into those with severity level (mild, moderate, severe) and death outcomes.

Results. VAERS received 10,007 reports after PCV13; 1,706 (17.0%) were serious. In 927 (9.3%), PCV13 was administered alone. The most frequently reported symptoms were pyrexia (26.4%), injection site erythema (15.3%) and irritability (14.6%). Injection site erythema (25.4%), injection site swelling (20.6%) and pyrexia (20.3%) were noted more commonly among children who were given PCV13 alone. The mean time from vaccination to start of symptoms was 1 day (range: day of vaccination – 2,033 days). There were 222 (2.2%) death reports with sudden infant death syndrome as the most common cause (37.8%). Pyrexia (45.1%), irritability (40.4%), and vomiting (39.7%) were most commonly reported among death reports. There were 20 (0.2%) reports of Kawasaki disease and 20 (0.2%) reports of anaphylaxis.

Conclusion. AEs reported to VAERS following PCV13 were consistent with AEs previously observed in licensure clinical trials and other post-licensure studies of PCV13. No new or unexpected patterns of AEs were identified.

Disclosures. All authors: No reported disclosures.

1489. Invasive Pneumococcal Disease in a Population with Underlying Comorbidities

Daniel Javorovsky, MD; Eitan Naaman Berezn, MD and Rodrigo José Sini De Almeida, MD, PhD, Pediatric, Santa Casa de Misericórdia de São Paulo, São Paulo, Brazil.

Background. Streptococcus pneumoniae (Spn) is a major cause of severe and life-threatening diseases in children and particularly among individuals with high-risk illnesses at all ages. As there is limited clinical data on IPD in high-risk patients and indirect effect of vaccination on the post-PCV10 era in developing countries, we’ve assessed the epidemiology of IPD in patients with and without underlying diseases before and after PCV10 introduction at Santa Casa de São Paulo (SCSP), Brazil.

Methods. We performed a prospective hospital-based surveillance study of patients with IPD from January 2000 to April 2017, including all cases of IPD (i.e. isolation of Spn from a normally sterile body fluid) among patients at all ages. Selected cases were stratified into 5 age groups to evaluate comorbidities and the effect of the PCV10 on different ages. Identified serotypes were grouped according to the available pneumococcal vaccines and further analyzed into pre-vaccination (2000–2009) and post-vaccination periods (2010–2017). Clinical information was extracted from patient’s records, then stratified based on their IPD risk profile. Ethical approvals to conduct the study were obtained from the SCSP institutional review board.

Results. 571 episodes were identified in 561 patients in all age groups, of which 440 (78.4%) had clinical data for analysis: 20.7% healthy, 79.3% had comorbidities. IPD decreased from 35.9 to 30.3 cases/year (-15.6%) at all ages after PCV10 introduction. Among healthy individuals and those with underlying comorbidities, annual cases counts decreased from 6.8 to 2.9 (57.3% reduction) and 18.6 to 20.5 cases/year (9.7% increase), respectively, between same periods; 30-day mortality through pre-vaccine period was 25% and 7.5% and in post-PCV10 period 27% and 8.7%, for comorbidity and healthy groups, respectively. IPD significantly decreased among healthy and comorbidity children ≤5y, with evidence of serotype replacement. Significant increase in bacteremia and pneumonia, also in serotypes included in all vaccines and NVT was evidenced at ages over 5y.

Conclusion. High rates of IPD have persisted in older subjects and in patients with underlying risk factors for IPD, despite children vaccination with PCV10. No herd effect was detected and serotype replacement is ongoing in this specific groups.

Disclosures. E. N. Berezin, Pfizer: Grant Investigator, Educational grant; R. José Sini De Almeida, Pfizer Inc: Employee, Salary

1490. Pneumococcal Vaccination Provides Substantial Value for Canadians

Francois Peloquin, BSc; Marie-Claude Breton, MPPharm; Matt Wasserman, MSc; Michele Wilson, MSPh; Cheryl McDade, BA and Raymond Farkough, PhD; Pfizer Canada, Kirkland, QC, Canada; Pfizer Inc, New York, New York; RTI Health Solutions, Research Triangle Park, North Carolina, Pfizer Inc, Collegeville, Pennsylvania

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Background. Introduction of pneumococcal conjugate vaccines (PCV) to the Canadian childhood routine immunization schedules (RIS) resulted in significant benefits. The 7-valent PCV was added to all provinces’ RIS between 2002 and 2006. The 10-valent PCV was used in Ontario and Quebec for 12 to 18 months in 2009 and 2010. The 13-valent PCV was marketed in 2010 and rapidly adopted by all provinces. Direct vaccine protection reduced incidence of invasive pneumococcal disease (IPD), pneumonia (PNE) and acute otitis media (AOM) in vaccinated children. Indirect vaccine protection also reduced the burden of disease (BOD) in other age groups.

Objective: To evaluate the economic impact of PCVs to Canadian society following nationwide RIS implementation.

Methods. Canadian databases and literature were reviewed to obtain pre- and post-PCV incidence of IPD, PNE and AOM, as well as direct and indirect medical costs (reported in 2017 $ CAD). Case counting index date was set to Jan 2005, at which point PCV RIS were implemented for over 90% of Canadians. A steady state scenario using weighted mean incidence rates was projected to Dec 2015 to estimate the number of cases without PCVs. Averted cases were obtained by subtracting the cases reported from the estimated case count without PCVs. Disease specific costs were assigned to averted cases and vaccine spend was subtracted from the total to obtain net savings to Canadian society.

Results. Successful implementation of PCV’s on the provinces’ RIS saved 2,365 lives and resulted in net savings of CAD $203 million between Jan 2005 and Dec 2015. These savings stem from averted direct and indirect medical costs associated with IPD, PNE and AOM cases.

Table 1 – BOD and related costs avoided by PCV use, 2005–2015

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<th>With PCVs</th>
<th>Without PCVs</th>
<th>Difference</th>
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<tbody>
<tr>
<td>Case count</td>
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<td></td>
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<tr>
<td>Bacteremia</td>
<td>27,041</td>
<td>36,808</td>
<td>-9,767</td>
</tr>
<tr>
<td>Meningitis</td>
<td>14,461</td>
<td>19,685</td>
<td>-5,224</td>
</tr>
<tr>
<td>Hospitalized PNE</td>
<td>366,927</td>
<td>386,413</td>
<td>-19,486</td>
</tr>
<tr>
<td>Nonhospitalized PNE</td>
<td>545,230</td>
<td>589,251</td>
<td>-44,021</td>
</tr>
<tr>
<td>AOM</td>
<td>3,629,952</td>
<td>3,744,476</td>
<td>-114,524</td>
</tr>
<tr>
<td>Costs ($ million)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Disease related</td>
<td>12,713</td>
<td>8,078</td>
<td>-4,635</td>
</tr>
<tr>
<td>Vaccine cost</td>
<td>9,783</td>
<td>9,783</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>31,496</td>
<td>17,861</td>
<td>-13,635</td>
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<tr>
<td>Other (no cost considered)</td>
<td></td>
<td></td>
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<tr>
<td>Mortality</td>
<td>36,917</td>
<td>39,282</td>
<td>-2,365</td>
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Conclusion. Introduction of PCV’s resulted in reduced pneumococcal burden of disease and net economic benefits to Canadian society.

Disclosures. F. Peloquin, Pfizer: Employee, Salary; M. C. Breton, Pfizer: Employee, Salary; M. Wasserman, Pfizer: Employee, Salary; M. Wilson, Pfizer: Consultant, Consulting fee; C. McDade, Pfizer: Consultant, Consulting fee; R. Farkough, Pfizer: Employee, Salary

1491. The Risk of Febrile Seizures Following Influenza and 13-Valent Pneumococcal Conjugate Vaccines

Meghan Baker, MD, ScD; Christopher Jankosky, MD, MPH; Katherine Yih, PhD, MPH; Susan Gruber, PhD; Lingling Li, PhD; Noelle Cocoros, DSc, MPH; Hana Lipowicz, MPH; Claudia Coronel-Moreno, MPH; Sandra Feibelmann, MPH; Nancy Lin, ScD; Cheryl McMahill-Walraven, PhD, MSW; David Menschik, MD, MPH; Mario Sevick, PhD; Nandini Selvam, PhD, MPH; Rong Chen Tileyne, MS; Lauren Zichittella, MS; Grace Lee, MD, MPH, FPIDS; and Alison Tse Kawai, ScD, SM; 1Department of Population Medicine, Harvard Pilgrim Health Care Institute and Harvard Medical School, Boston, Massachusetts, 2Brigham and Women’s Hospital, Boston, Massachusetts, 3FDA Center for Biologics Evaluation and Research, Silver Spring, Maryland, 4Sanofi Genzyme, Cambridge, Massachusetts, 5Optum Epidemiology, Boston, Massachusetts, 6Aetna, Blue Bell, Pennsylvania, 7Comprehensive Health Insights, Sugar Land, Texas, 8QuintilesIMS, Fairfax, VA, 9Division of Infectious Diseases, Boston Children’s Hospital, Boston, Massachusetts

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Background. Evidence on the risk of febrile seizures (FS) after vaccination with inactivated influenza (IIV) and 13-valent pneumococcal conjugate vaccine (PCV13) is mixed. Among children 6–23 months, we examined the risk of FS following IIV and PCV13 during the 2013–14 and 2014–15 influenza seasons, for which vaccine virus strains were the same.
Methods. We used claims data from 4 large national insurers in the FDA-sponsored Sentinel Initiative, which was developed to monitor the safety of FDA-regulated medical products. With a self-controlled risk interval design, the risk of FS in 0–1 days following IV and following PCV13 was compared with a comparison interval (14–20 days), adjusting for confounding by age, calendar time, and concomitant vaccination with the other vaccine. In exploratory analyses, we assessed whether the effect of IV is modified by concomitant administration of PCV13.

Results. During the study period, 355,486 children received IV and 581,868 received PCV13. We observed an incidence rate ratio (IRR) of 1.12 (95% CI 0.80, 1.56) for the risk of FS following IV after adjustment for age, calendar time and concomitant PCV13. PCV13 was associated with an increased risk of FS (IRR adjusted for age, calendar time and concomitant IV, 1.80, 95% CI 1.29, 2.52). The attributable risk for PCV13 ranged from 0.3 to 5.16 per 100,000 doses.

The age and calendar-time adjusted IRR comparing exposed time to unexposed time was greater for concomitant IV and PCV13 (IRR 2.80, 95% CI 1.63, 4.83), as compared with that for PCV13 without concomitant IV (IRR 1.54, 95% CI 1.04, 2.28). However, the formal test assessing for interaction between IV and PCV13 was not statistically significant.

Conclusion. We found an elevated risk of FS after PCV13 vaccine but not after IV, when adjusting for concomitant administration of the other vaccine. We found some evidence to suggest that concomitant administration of IV with PCV13 might impact the independent effects of PCV13, but the study was not powered to assess this interaction. The risk of seizures associated with PCV13 is low compared with a child’s lifetime risk of FS. Findings should be interpreted in the context of the importance of preventing influenza and pneumococcal infections in young children.

Disclosures. L. Li, sanofi pasteur: The author is currently employed by Sanofi Genzyme, which shares the same parent company as sanofi pasteur, the manufacturer of the Flu vaccine. However, the work was done while this author was still employed by Harvard Pilgrim Health Care Institute. No financial benefit received

190. Background and Travel expenses; Pfizer: Grant Investigator and Scientific Advisor, Research grant and covered by the 23-valent polysaccharide vaccine.

192. Type coverage is diminishing year after year but a majority of cases remains potentially preventable.

2 primary PCV13 doses but not the toddler booster dose, which suggests a window of susceptible carriers.

3 doses. Epidemiological years were from July through June.

Overall, high APRs were seen throughout the study. A total of 226,035 antibiotic prescriptions were dispensed. Overall annual APR means (per 1,000 ≤ 3 SD) were 2068.9 ± 15.2 and 1841.1 ± 39.1 in 2005–2009 and 2013–2016, respectively (11% reduction; 95% CI 10–12%) (Figure 1). Amoxicillin, the most commonly prescribed antibiotic drug (60.8% of all prescriptions) was reduced by 14% (95% CI 13–15%) (Figure 2). Similar reductions were seen for oral cephalosporins and amoxicillin/clavulanate. However antibiotic use remained continuously throughout the study. Calculation of linear trends before and after PCV implementation demonstrated a significant change in trends for amoxicillin, oral cephalosporin and total APRs, strongly suggesting a causative role of PCVs. PCV implementation resulted in an overall reduction of 45,320 prescriptions for a cohort of 100,000 children during their first 2 years of life (95% CI 41,212 to 49,007).

Conclusion. A clear and significant change in all APR trends associated with PCV implementation was observed in children <24 months old with a baseline high APR. This resulted in a marked decline in antibiotic use. Continuous surveillance is needed to determine further trends, including those for specific antibiotic categories.

194. Antibiotic Prescription Rates in Children <24 Months Old Following PCV7/ PCV13 Sequential Implementation

193. This resulted in a marked decline in antibiotic use. Continuous surveillance is needed to determine further trends, including those for specific antibiotic categories.