Effect of Introduction of Pneumococcal Conjugate Vaccine Immunization on Nasopharyngeal Colonization of Streptococcus pneumoniae in South Africa

Abstract

Introduction

Pneumococcal conjugate vaccine (PCV) immunization of children decreases their risk of nasopharyngeal acquisition of vaccine serotypes and concurrently reduces the transmission thereof to PCV-unvaccinated age groups. We studied the impact of routine infant PCV immunization at population level, on the epidemiology of nasopharyngeal pneumococcal colonization in a rural (Agincourt) and an urban (Soweto) South African community with high prevalence of HIV-infection. Furthermore, we delineated the effect of infant PCV immunization on bacterial interactions of Streptococcus pneumoniae with Haemophilus influenzae and Staphylococcus aureus at the population level. Lastly, we assessed the utility of colonization data to predict the impact of childhood PCV immunization on the direct and indirect effect against invasive pneumococcal disease (IPD).

Materials and Methods

A series of cross sectional colonization surveys were undertaken (in Agincourt and Soweto) between 2009 and 2012. These years were representative of the pre- or early-PCV-era and PCV-era years. The seven valent PCV (PCV7) was introduced into the South African national immunization program in April 2009, using a 6, 14 and 40 weeks of age dosing schedule with no catch up campaign of older children. Subsequently, PCV7 was replaced by 13-valent PCV (PCV13) in May 2011, with a limited catch up campaign.

Nasopharyngeal swabs were collected among household members and mother-infant pairs and processed for S. pneumoniae, H. influenzae and S. aureus using standard microbiologic techniques. Additionally, the trends in incidence of IPD for 2005 to 2012 were evaluated. Multivariate logistic regressions were performed to assess the impact of PCV on carriage in different age groups. Adjusted risk ratios (aRR) or adjusted odds ratios (aOR) are reported as measures of impact and association. We compared the predicted changes in IPD among children and their mothers, stratified by HIV, using a theoretical model and compared this to the observed changes in IPD.

Results

Among rural households, the prevalence of PCV7-serotype colonization among all ages decreased from 18.3% in 2009 to 11.4% in 2011; $p<0.0001$. This included reductions (adjusted risk ratio; aRR) of 50% (95% Confidence Interval [95%CI]:0.42-0.59), 34% (95%CI: 0.48-0.92) and 64% (95%CI: 0.18-0.74) in age-groups <2 years, 6-12 years and adults, respectively. The prevalence of PCV7 serotype colonization among primary caregivers decreased from 10.2% in 2009, to 5.4% in 2011, ($p<0.001$).

Non-vaccine serotype colonization prevalence increased by 35% (95%CI: 1.17-1.56) among children <2 year of age in 2011, however, it declined by 45%-54% among adolescents and adults.

In urban mother-infant pairs, PCV13serotype colonization decreased from 2010 compared to 2012 among HIV-uninfected (aOR: 0.32; 95%CI: 0.25-0.40) and HIV-infected children (aOR: 0.37; 95%CI: 0.28-0.49), whilst there was an increase in non-vaccine serotype colonization. Decreases in PCV13 serotype colonization were also observed in HIV-uninfected women (aOR: 0.44; 95%CI: 0.23-0.81); with a similar trend in HIV-infected women. Non PCV13 serotype colonization declined in 2012 compared to in 2010 among HIV-infected women (aOR: 0.69, 95%CI: 0.48-0.99). HIV-infected compared to HIV–uninfected women had higher prevalence of overall (20.5% vs. 9.7% in 2010; 13.8% vs. 9.7% in 2012) and PCV13 serotype colonization (8.7% vs. 5.4% in 2010; 4.8% vs. 2.0% in 2012) in both sampling periods; p<0.04 for all observations.

For bacterial associations in the rural population, from 2009 to 2011 in children 0-2 years and 3-12 years of age, the prevalence of overall S. pneumoniae colonization decreased from 74.9% to 67.0% (p<0.001). Although there was also a decrease in prevalence of H. influenzae colonization in the 3-12 year age group (55.1% to 45.3%, p<0.001), this was not evident among those <2 years of age. The prevalence of S. aureus colonization remained unchanged in all childhood age groups. In individuals older than 12 years of age, the prevalence of colonization decreased for all studied bacteria including S. pneumoniae (11.2% vs 6.8%), H. influenzae (16.7% vs. 8.8%) and S. aureus (31.2% vs. 23.7%); p<0.001 for all comparisons.

Analysing the colonization and IPD findings, between the pre PCV era (2007-2009) and the PCV13 era (2012), we observed reductions in vaccine serotype colonization and IPD due to PCV7 serotypes and the additional six serotypes included in PCV13 among children and women. Using the changes in vaccine serotype colonization over time, the hypothetical model accurately predicted changes in vaccine-serotype IPD incidence compared to the observed changes in PCV-unvaccinated HIV-infected and HIV-uninfected adults; and among children too old to have been immunized. The model, however, underestimated the reduction in vaccine serotype IPD among the child age-group targeted for immunization. The model was, however, not useful in predicting the changes that occurred for non vaccine serotypes either among PCV-vaccinated or PCV-unvaccinated age-groups.

Discussion and Conclusion

Infant PCV immunization resulted in population wide decreases in vaccine-serotype colonization of S. pneumoniae including among HIV-infected adults in both rural and urban settings. Surveillance of colonization prior and following childhood PCV immunization can be used to infer indirect effects against vaccine-serotype IPD in the community even in high HIV-prevalence settings such ours.