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Short Communication

Prevalence of nasopharyngeal pneumococcal colonization in children and antimicrobial susceptibility profiles of carriage isolates



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SUMMARY

Nasopharyngeal (NP) pneumococcal carriage predisposes children to pneumococcal infections. Defining the proportion of pneumococcal isolates that are antibiotic-resistant enables the appropriate choice of empiric therapies. The antibiogram of NP carriage isolates derived from a pediatric population following the introduction of the 13-valent pneumococcal conjugate vaccine was defined in this study.

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1. Introduction

Nasopharyngeal (NP) colonization by *Streptococcus pneumoniae* predisposes young children to acute otitis media (AOM) and invasive pneumococcal disease.^{1,2} The introduction of the seven-valent pneumococcal conjugate vaccine (PCV7) in 2000 significantly increased the proportion of penicillin-susceptible pneumococcal isolates (defined as a penicillin MIC ≤ 0.06 $\mu\text{g/ml}$) isolated from NP carriers in the pediatric population of St. Louis, Missouri, USA.³ The definition of a high proportion of penicillin-susceptible isolates confirmed the appropriate use of low-dose amoxicillin (40–45 mg/kg per day) as first-line therapy for AOM in 2006.^{3,4} Recently the American Academy of Pediatrics (AAP) has recommended ‘high-dose’ amoxicillin (90 mg/kg per day) as first-line therapy for AOM because of increasing penicillin resistance.⁴ The new guidelines

posit that the 13-valent PCV (PCV13) may result in a reduced prevalence of antibiotic resistance among disease-causing pneumococcal isolates.⁴

A pneumococcal colonization prevalence study was performed in the same geographic region as the 2006 study to evaluate trends in penicillin resistance following the introduction of PCV13 in 2010. The objectives were to evaluate the prevalence of NP pneumococcal colonization and to assess the antimicrobial susceptibility profiles of pneumococcal isolates recovered.

2. Methods

Following approval by the Washington University Human Research Protection Office, informed consent for participation was obtained from the parents/legal guardians of otherwise healthy children aged 0–17 years requiring anesthesia for minor procedures (e.g., herniorrhaphies) in the St. Louis Children’s Hospital Same Day Surgery center.⁵ Children with a chronic illness, such as a primary immunodeficiency or cystic fibrosis, were excluded. Children were also excluded if they were receiving an antibiotic,

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or if they had an upper respiratory infection, a fever, had been admitted to hospital within the preceding 24 h, or had been enrolled previously. Vaccination coverage was determined by obtaining records from primary care pediatricians.

A single NP swab (E-swab Minitip, Copan) was obtained, and eluate (100 μ l) was inoculated directly into 5% sheep blood agar plates (BAP; BD Biosciences). To enrich for pneumococcus, 100 μ l of eluate was also inoculated into 3 ml Todd–Hewitt broth (BD Biosciences) containing 0.5% yeast extract (THY) and 0.5 ml rabbit serum. After incubation, 100 μ l of inoculated broth was streaked directly onto BAP. Following overnight incubation at 35 °C in 5% CO₂, up to 12 α -hemolytic colonies were selected for analysis. Gram-positive cocci in pairs and chains were determined to be pneumococci if they were catalase-negative, optochin-susceptible, and bile-soluble.³

Antibiotic susceptibility testing was performed in the Microbiology Laboratory at St. Louis Children's Hospital.⁶ The minimum inhibitory concentrations (MICs) of penicillin and cefotaxime were determined by gradient diffusion (Etest, bioMérieux). Susceptibilities to erythromycin, clindamycin, sulfamethoxazole/trimethoprim, vancomycin, levofloxacin, and linezolid were determined by Kirby–Bauer disk diffusion.

Chi-square analyses were performed in GraphPad Prism. Confidence intervals (CI) were determined using the Wilson procedure for calculating the 95% CI for a binomial proportion.

3. Results

During a 1-year period (July 2013 to June 2014), 218 children were enrolled, of whom 40 (18.3%; 95% CI 14–24%) were colonized with pneumococcus (Table 1). The prevalence of pneumococcal colonization of children <2 years of age was 37% (95% CI 24–53%), of children aged 2–6 years was 32% (95% CI 22–44%), and of children \geq 7 years was 2.7% (95% CI 1–8%; $p < 0.0001$ by Chi-square test). The overall prevalence of colonization in children aged 6 years or younger was 34% (37 children colonized of 109 enrolled; 95% CI 26–43%). There was no significant correlation between receipt of three or more PCV vaccines and colonization (data not shown).

The antimicrobial susceptibility profile (antibiogram) of the 40 carriage isolates recovered was determined (Table 1, Figure 1^{6,7}). A statistically valid antibiogram requires a minimum of 30 isolates, as per guidelines established by the Clinical and Laboratory Standards Institute.⁷ To enable direct comparison to the earlier St. Louis study, the percentage of isolates with a penicillin MIC ≤ 0.06 μ g/ml was calculated (Table 1).⁸ There was no significant difference in penicillin susceptibility in the different age groups, and it was found that 20 (50%; 95% CI 35–65%) of the current isolates had a penicillin MIC of ≤ 0.06 μ g/ml (Table 1).

Table 1

Prevalence of nasopharyngeal pneumococcal colonization in children in the greater St. Louis area^a

Age, years	Enrolled	Colonized (%; 95% CI)	Penicillin MIC ≤ 0.06 μ g/ml (%; 95% CI)
<2	41	15 (37%; 24–52%)	8 (53%; 30–75%)
2–6	68	22 (32%; 22–44%)	10 (45%; 27–65%)
≥ 7	109	3 (2.7%; 1–8%) ^b	2 (67%; 21–94%)
Total	218	40 (18.3%; 14–24%)	20 (50%; 35–65%)

CI, confidence interval; MIC, minimum inhibitory concentration.

^a The numbers of children enrolled and colonized are shown, grouped by age. Half of the nasopharyngeal isolates demonstrated penicillin MICs of ≤ 0.06 μ g/ml. Categorization of current isolates using the susceptibility criteria in use before 2006 allows direct comparison of the present findings to those reported previously in our region.³

^b Prevalence is significantly lower in children aged ≥ 7 years than in children <7 years old; $p < 0.0001$.

Finally, the antibiotic susceptibility profiles of the colonizing isolates were compared to those of invasive pneumococcal isolates recovered from clinical specimens (blood, cerebrospinal fluid, tracheal aspirates, and bronchoalveolar lavage specimens) at St. Louis Children's Hospital⁶ (Figure 1). The antibiotic susceptibility profile of colonizing isolates was similar to the 2012 and 2013 profiles of invasive isolates (Figure 1). The only significant difference between colonizing and invasive isolates was the percentage of colonizing isolates that were penicillin-susceptible under non-meningitic conditions using intravenous administration (PCN-S-NM; $p = 0.038$).

4. Discussion

The present study is consistent with other studies indicating that PCV does not reduce the overall pneumococcal carriage prevalence.^{1,2,9} It was found that the prevalence of pneumococcal colonization in children under 7 years of age has not been reduced from the prevalence of 39% identified in the prior study (129 children colonized of 327 enrolled; 95% CI 26–43%).³ There was also no increase in penicillin susceptibility following the introduction of PCV13, as the proportion of isolates with a penicillin MIC ≤ 0.06 μ g/ml (50%) was lower than the proportion of 67% found previously.³ The stable prevalence of pneumococcal colonization and unchanged proportion of isolates with a penicillin MIC ≤ 0.06 μ g/ml were observed even though the study populations were slightly different; children with symptoms of an upper respiratory infection (URI) were excluded in the present study, while they were included in the prior study.³ As URI symptoms are a risk factor for pneumococcal colonization,² a lower prevalence in the present study might have been expected based on this

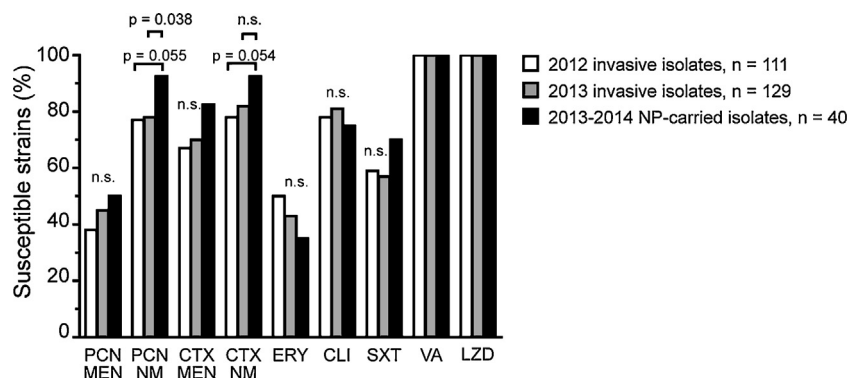


Figure 1. Percentage of nasopharyngeal colonizing and invasive isolates susceptible to the antibiotics indicated, defined in the 2014 Clinical and Laboratory Standards Institute guidelines^{6,7}. PCN, penicillin; CTX, cefotaxime; ERY, erythromycin; CLI, clindamycin; SXT, sulfamethoxazole/trimethoprim; VA, vancomycin; LZD, linezolid; MEN, meningitic breakpoint (PCN MIC ≤ 0.06 μ g/ml, CTX MIC ≤ 0.5 μ g/ml); NM, non-meningitic breakpoint (PCN MIC ≤ 2 μ g/ml, CTX MIC ≤ 1 μ g/ml).

population difference. The results of this study are in contrast with those of recent studies performed in Israel and Atlanta, Georgia, USA, in which receipt of PCV13 increased the proportion of penicillin-susceptible isolates among colonizing isolates.^{2,10} Colonizing isolates found in St. Louis were also more resistant to penicillin than those in a recent cross-sectional study performed in Milan.¹ Higher penicillin MICs of NP pneumococci in St. Louis compared to those in other areas may be due to greater antibiotic use in the USA, although confirmation of a causal relationship requires further study.

With the exception of a slightly higher prevalence of β -lactam-susceptible colonizing isolates, the antibiotic susceptibility profiles of colonizing isolates closely approximate those of invasive isolates, demonstrating that population surveys of colonizing isolates can be used to determine the local choice of empiric antibiotic therapy.

In summary, the prevalence of pneumococcal colonization in the pediatric population of the St. Louis area was surveyed, finding no change in prevalence and, more importantly, no evidence of an increasing prevalence of penicillin-susceptible isolates following the introduction of PCV13.

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Conflict of interest: The authors have no financial conflicts of interest to declare.

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