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Nasopharyngeal carriage of *Streptococcus pneumoniae* in very low birth weight infants after administration of heptavalent pneumococcal conjugate vaccine

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Introduction

The effect of pneumococcal conjugate vaccine-7 **(**PCV-7) in reducing pneumococcal nasopharyngeal (NP) carriage in very low birth weight (VLBW) infants has not been studied. Our primary objective was to characterize NP carriage of *S. pneumoniae* in a group of VLBW infants (401-1500 grams) before administration of first PCV-7 (PRE) and at 4-6 weeks after a 3-dose PCV-7 primary series (POST). We also investigated the correlation between vaccine induced pneumococcal IgG antibody level and pneumococcal NP carriage POST PCV-7.

Methods

VLBW infants participating in a PCV-7 immunogenicity study[1] were enrolled from 4 NICHD Neonatal Research Network (NRN) sites (Detroit, MI, Rochester, NY, Dallas, TX and Birmingham, AL). The study was approved by NRN and each site's institutional review board. Written informed consent was obtained from each subject's parent/guardian. Infants received PCV-7 at approximately 2, 4 and 6 months of age.

NP cultures were obtained at the PRE and POST visits. Antimicrobial susceptibility testing of all pneumococcal isolates was performed.

Pneumococcal isolates were serotyped at the Centers for Disease Control and Prevention, Atlanta, GA. Serotypes 4, 6B, 9V, 14,18C, 19F, and 23F were classified as vaccine serotypes (VT). Other serotypes were classified as non-VT (NVT).

Anti-pneumococcal antibodies[2] against seven VT were measured at POST visit and ≥0.15μg/ml was chosen as a possible measure of protective level.[3]

Descriptive statistics were used to characterize the study subjects with regard to birth weight, gestational age at birth (GA) and chronologic age (CA) at swab collection, as well as serotype and antimicrobial susceptibilities of pneumococcal isolates.

Results

123 of 135 infants enrolled had at least one NP swab obtained; 71 had PRE and 102 had POST NP swab cultures. 50 infants had both PRE and POST NP swabs. Most (44/71=62%) had PRE NP swab done while in NICU, whereas all but one had POST NP swab done after hospital discharge.

The median GA of 123 infants was 28 weeks (range 23-32). The median CA at PRE and POST NP swab collections were 2 months (range 1-3) and 8 months (range 6-10) respectively.

S. pneumoniae was isolated in 4.2% (3/71) PRE and 12.7% (13/102) POST samples. One infant had positive PRE and POST NP cultures with 2 different serotypes; another colonized at PRE had a negative POST NP culture. Among the 50 infants with both PRE and POST NP swabs, 49 had negative PRE NP cultures of whom 8 became colonized at POST (all NVT) (Table 1).

Serotyping was done on 15 of 16 isolates (Table 1). One PRE isolate was a VT; all 12 POST isolates were NVT. Antibiotic susceptibility (Table1) showed one PRE isolate resistant to erythromycin. Of 12 POST isolates, 2 (19A) were resistant to 4 antibiotics, 1 (35B) resistant to penicillin and 1 (non-typeable) resistant to erythromycin.

Serum anti-capsular IgG antibody levels to 7 VT were available for 100 infants who had POST NP swabs. Anti-pneumococcal antibody ≥0.15 μg/ml were achieved in 88-99% and varied by serotype. Since all POST pneumococcal isolates were NVT, assessment of NP carriage status based on antibody levels could not be performed.

Comment

The pneumococcal NP carriage rate of 12.7 % in our VLBW infants post-PCV-7 vaccination was lower than previously reported during the pre-PCV-7[4] and early post-PCV-7[5] eras and was exclusively due to NVT. Our findings also support the recent observation that NVT serotype 19A is becoming more prevalent. An expanded PCV such as PCV-13 which includes 6 additional serotypes (1, 3, 5, 6A, 7F and 19A) may change that. Regardless of serum pneumococcal anti-capsular antibody levels, all POST pneumococcal NP isolates were NVT, suggesting protection against VT NP carriage at 4-6 weeks POST period.

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Data collected at participating NRN sites were transmitted to Research Triangle Institute (RTI) International, the data coordinating center (DCC) for the NRN, which stored, managed, and analyzed the data for this study.

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Table 1

Pneumococcal nasopharyngeal (NP) isolates: time and place of collection, birth weight, serotype and antimicrobial susceptibility

NP swab collection time[a]	NP Swab collection place[b]	Post-discharge days when NP swab was obtained[c]	Birth weight in grams	Serotype[d]	Penicillin MIC[e] μg/ml	Ceftriaxone MIC[e] μg/ml	Erythromycin MIC[e] μg/ml	Clindamycin MIC[e] μg/ml
Pre	NICU	-55 (still in NICU)	1035	Non-typeable	0.12 (I)	0.03 (S)	32 (R)	0.12 (S)
Pre[f]	PCP	10	1100	38	0.03 (S)	0.03 (S)	0.25(S)	0.25 (S)
Pre	PCP	50	1450	19F	0.03 (S)	0.016 (S)	0.25(S)	0.5 (I)
Post[f]	PCP	166	1100	35B	2 (R)	1 (S)	0.06 (S)	0.06 (S)
Post	PCP	122	750	10A	0.03 (S)	0.03 (S)	0.25 (S)	0.12 (S)
Post	PCP	168	1185	35F	0.03 (S)	0.03 (S)	0.25 (S)	0.12 (S)
Post	PCP	189	1230	19A	2 (R)	2 (I)	>256 (R)	>256 (R)
Post	PCP	139	910	19A	0.12 (I)	0.12 (S)	0.25 (S)	0.25 (S)
Post	PCP	120	925	19A	2 (R)	2 (I)	>256 (R)	>256 (R)
Post	PCP	189	1480	Non-typeable	0.38 (I)	0.06 (S)	16 (R)	0.125 (S)
Post	PCP	238	1405	6A	0.06 (S)	0.12 (S)	0.25 (S)	0.25 (S)
Post	PCP	235	1365	6A	0.12 (I)	0.12 (S)	0.25 (S)	0.25 (S)
Post	PCP	159	1216	38	0.06 (S)	0.03 (S)	0.12 (S)	0.25 (S)
Post	PCP	208	1286	15C	0.03 (S)	0.016 (S)	0.25 (S)	0.5 (I)
Post	PCP	182	680	23A	0.06 (S)	0.03 (S)	0.25 (S)	0.25 (S)
Post	PCP	182	650	N/A[g]	N/A[g]	N/A[g]	N/A[g]	N/A[g]

[a]Before the first heptavalent pneumococcal conjugate vaccine (PCV-7) dose (PRE) ; 4-6 weeks after the third PCV-7 dose (POST).

[b]Neonatal Intensive Care Unit (NICU) or Primary Care Provider's (PCP) office.

[c]The13 POST isolates were recovered at a median of 179 days after hospital discharge (range 120-238 days).

[d]Serotyped at the *Streptococcus* Laboratory of Centers for Disease Control and Prevention (CDC), Atlanta, GA using latex agglutination and confirmation by quellung reaction with type-specific pneumococcal antisera.

[e]E-test method (AB Biodisk, Solna, Sweden); Minimum inhibitory concentration (MIC) in μg/ml, interpreted as: susceptible (S), intermediate (I) and resistant (R).[6]

[f] The same infant.

[g] Isolate not viable for further testing.