Vaccine 28 (2010) 7583–7588

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Short communication

The association of ethnicity with antibody responses to pneumococcal vaccination among adults with HIV infection☆

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ARTICLE INFO

Article history:
Received 14 July 2010
Received in revised form 7 September 2010
Accepted 14 September 2010
Available online 29 September 2010

Keywords:
Ethnicity
Antibodies
Pneumococcal vaccination
HIV

ABSTRACT

Ethnicity may be associated with the incidence of pneumococcal infections and the frequency of protective vaccine responses. Earlier studies have suggested that HIV-infected persons of black ethnicity develop less robust immune responses to pneumococcal vaccination that may relate to their higher incidence of invasive disease. We evaluated the association of ethnicity with capsule-specific antibody responses to pneumococcal revaccination, with either the pneumococcal conjugate (PCV) or polysaccharide (PPV) vaccines among 188 HIV-infected adults. The proportion of the 77 African Americans (AA) and 111 Caucasians with comparable virologic and immunologic parameters who achieved a positive immune response (≥2-fold rise in capsule-specific IgG from baseline with post-vaccination value ≥1 μg/mL for ≥2 of 4 serotypes) at day 60 after revaccination was similar (43% vs. 49%, respectively, $p = 0.65$). Results were also similar when vaccine types (PPV and PCV) were examined separately. Mean changes in $\log_{10}$ transformed IgG levels from baseline to days 60 and 180 post-vaccination were also not significantly different between AA and Caucasians. In summary, in this ethnically diverse cohort with equal access to care, we did not observe differential antibody responses between AA and Caucasian HIV-infected adults after pneumococcal revaccination.

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1. Introduction

Streptococcus pneumoniae infections are a common cause of morbidity among persons infected with the human immunodeficiency virus (HIV) [1–7]. Several studies have demonstrated an ethnic disparity among rates of pneumococcal disease with an increased risk among blacks compared with whites in both the general population and persons infected with HIV [3,8–12].

The efficacy of pneumococcal vaccinations in preventing invasive pneumococcal disease among HIV-infected adults is suboptimal in all ethnic groups [6]. A limited IgG antibody response to pneumococcal capsular polysaccharides, an important determinant of disease and protection, among black Americans and Africans has been proposed to contribute to the higher risk of disease in this ethnic group [12,13]. However, the exact nature of this proposed poor vaccine efficacy is unclear as little data are available that directly compare antibody levels generated post-vaccination among HIV-infected persons of differing ethnicities. Therefore, we utilized data from a prospective, randomized study to compare capsule-specific IgG levels prior to and following pneumococcal

☆ Part of these data was presented at the XVIII International AIDS Conference, Vienna, Austria, July 18–23, 2010.

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0264-410X/$ – see front matter. Published by Elsevier Ltd.
doi:10.1016/j.vaccine.2010.09.056

Table 1
Baseline characteristics of study population by ethnicity.

Characteristic	Total cohort $N = 188$	African Americans $N = 77$	Caucasians $N = 111$	p-Value
Demographics				
Age, years (median, IQR)	42 (36–47)	42 (35–48)	42 (37–46)	0.92
Gender, male (N, %)	178 (94.7%)	71 (92.2%)	107 (96.4%)	0.21
History of prior pneumococcal vaccination and pneumonia				
No. of previous PPVs (median, IQR)	1 (1–2)	1 (1–2)	1 (1–2)	0.70
Time since last PPV, years (median, IQR)	4.5 (3.6–6.0)	4.5 (3.7–5.9)	4.7 (3.5–6.1)	0.95
History of pneumonia[a] (N, %)	33 (17.6%)	8 (10.4%)	25 (22.5%)	0.03
HIV-related history				
Duration of HIV infection, years (median, IQR)	9.5 (4.7–16.0)	9.3 (4.4–16.3)	9.5 (5.1–15.4)	0.92
$CD4^+$ T cell count, cells/mm^3 (median, IQR)	540 (391–701)	550 (390–711)	532 (392–692)	0.76
$CD4^+$ percentage, % (median, IQR)	30 (23–36)	30 (23–35)	30 (24–37)	0.45
Plasma HIV RNA, % undetectable (≤400 copies/mL)	143 (76.5%)	58 (75.3%)	85 (77.3%)	0.76
Plasma HIV RNA, $\log_{10}$ copies/mL (median, IQR)	1.7 (1.7–2.4)	1.7 (1.7–2.5)	1.7 (1.7–2.3)	0.88
Receipt of HAART[b], (N, %)	153 (81.4%)	60 (77.9%)	93 (83.8%)	0.31
Treatment allocation during original study				
Received PCV during study, (N, %)	121 (64.4%)	50 (64.9%)	71 (64.0%)	0.89

p-Values comparing proportions were calculated using Chi-square tests, and p-values comparing medians were calculated using Kruskal–Wallis, tests.
[a] Type of pneumonia not specified.
[b] Highly active antiretroviral therapy as defined by treatment guidelines.

revaccination in African American (AA) and Caucasian HIV-infected adults.

2. Methods

2.1. Study population

We performed subgroup analyses of capsule-specific IgG responses among AA and Caucasians from a randomized study comparing the immunogenicity of revaccination with pneumococcal conjugate vaccine (PCV) to pneumococcal polysaccharide vaccine (PPV) among HIV-infected adults previously vaccinated with PPV. The main study evaluated 204 HIV-infected adults who were randomized (2:1) to PCV (Prevnar, Wyeth Pharmaceuticals, $n = 131$) or PPV (Pneumovax, Merck & Co., Inc., $n = 73$) between February 2006 and September 2008 [14].

Of all study participants, 77 were AA and 111 Caucasians, and these subjects are the focus of this sub-analysis. Data on ethnicity was based on self report. Study participants were infected with HIV (documented by a positive ELISA with Western Blot confirmation), between ages 18 and 60 years, had received a prior PPV vaccination 3–8 years earlier, and without significant concurrent medical conditions except for HIV infection. All participants were military beneficiaries who have open and free access to healthcare, and low rates of illicit drug use [15]. Study subjects provided written informed consent, and the study was approved by the governing institutional review boards and registered with the Clinical Trials network (registration NCT00622843).

2.2. Study design and procedures

The primary study outcome was achieving a positive immune response, defined as a ≥2-fold rise in capsule-specific IgG with post-vaccination value ≥1 μg/mL, at day 60 post-vaccination for at least 2 of 4 serotypes. The endpoint was chosen in concordance with prior reports, and a threshold value of 1 μg/mL was used to assure that fold rises represented meaningful post-vaccination antibody levels [16,17]. Secondary outcomes included positive IgG responses and changes in capsule-specific IgG concentrations for each serotype at each time point.

Pneumococcal vaccines were administered intramuscularly (0.5 ml) in the deltoid muscle using a 23-gauge, 1-inch needle in accordance with manufacturers' guidelines. Serum samples were collected at baseline (1–21 days prior to revaccination) and days 14, 60, and 180 after revaccination. We determined the capsule specific IgG levels to four pneumococcal serotypes (4, 9V, 14, and 19F), which represented a range of important serotypes among HIV-associated pneumococcal infections.

2.3. Assays

Serotype-specific pneumococcal IgG concentrations were measured by ELISA, as previously described [14,18]. In brief, sera were preadsorbed with 4 μg/mL of cell wall polysaccharide and 2 μg/mL of type 22F capsular polysaccharide overnight to eliminate non-capsule-specific antibodies [19,20]. Capsular polysaccharides were adhered to 96-well microtiter plates, and capsule-specific IgG was detected with affinity-purified horseradish peroxidase-conjugated goat anti-human IgG label and appropriate substrates. Samples

Table 2
Capsule-specific IgG levels (μg/mL) at baseline (prevaccination) and at days 14, 60, and 180 post-vaccination among African Americans and Caucasians.

	African Americans		Caucasians		p-Value
	N.	Median (IQR)	N.	Median (IQR)	
Serotype 4					
Day 0	75	0.28 (0.11, 0.73)	108	0.29 (0.10, 0.70)	0.83
Day 14	72	0.83 (0.29, 1.73)	107	0.89 (0.32, 4.33)	0.12
Day 60	68	0.79 (0.25, 2.39)	105	0.72 (0.30, 3.35)	0.84
Day 180	66	0.73 (0.31, 1.78)	102	0.79 (0.28, 2.03)	0.89
Serotype 9V					
Day 0	75	0.59 (0.28, 1.74)	108	0.46 (0.20, 1.19)	0.16
Day 14	72	1.52 (0.60, 3.97)	107	2.24 (0.68, 5.67)	0.19
Day 60	68	1.72 (0.58, 3.88)	105	2.04 (0.69, 6.14)	0.37
Day 180	66	1.30 (0.40, 3.33)	102	1.38 (0.44, 4.10)	0.55
Serotype 14					
Day 0	75	0.97 (0.42, 5.00)	108	0.60 (0.24, 3.59)	0.21
Day 14	72	2.82 (0.80, 10.41)	107	2.56 (0.80, 9.32)	0.81
Day 60	68	2.52 (0.75, 9.91)	105	2.88 (0.67, 12.87)	0.98
Day 180	66	2.76 (0.67, 7.14)	102	3.28 (0.65, 7.62)	0.67
Serotype 19F					
Day 0	75	0.83 (0.33, 1.82)	108	0.53 (0.26, 1.71)	0.14
Day 14	72	0.97 (0.41, 3.30)	107	0.95 (0.38, 3.16)	0.91
Day 60	68	1.19 (0.44, 3.26)	105	0.85 (0.34, 2.42)	0.28
Day 180	66	0.94 (0.41, 2.36)	102	1.02 (0.37, 2.33)	0.89

p-Value is from Kruskal–Wallis test comparing African Americans to Caucasians. IQR, interquartile range; N, number.