Protective effect of PCV vaccine against experimental pneumococcal challenge in adults is primarily mediated by controlling colonisation density

P16

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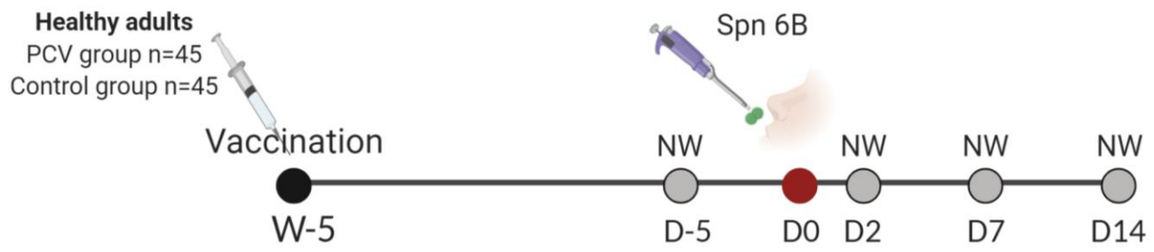
BACKGROUND AND AIMS

Widespread use of Pneumococcal Conjugate Vaccines (PCV) has resulted in a reduction in nasopharyngeal colonisation and invasive pneumococcal disease caused by vaccine-type serotypes. In a double-blind, randomised controlled trial using the Experimental Human Pneumococcal Challenge (EHPC) model, PCV-13 (Prevenar-13) conferred 83% protection against colonisation acquisition of *S. pneumoniae* serotype 6B and a reduction in bacterial intensity in experimentally colonised volunteers as measured by classical culture.

We used a qPCR approach to re-assess volunteer samples from our PCV study for experimental colonisation of 6B pneumococcus.

METHODS

PCV/EHPC Clinical trial



DNA extraction

DNA was extracted from nasal wash bacterial pellets using the Agowa mag Mini DNA isolation kit

Multiplex qPCR

We developed a novel multiplex qPCR based on methods previously published, using partial amplification of *lytA* and 6A/B *cpsA* genes. DNA from BHN418 serotype 6B, serially diluted 1:10 from 4.14×10^6 copies, was used as a standard curve. A sample was considered positive if at least one duplicate had a CT value less than 40.

RESULTS

Colonisation acquisition rates by molecular methods

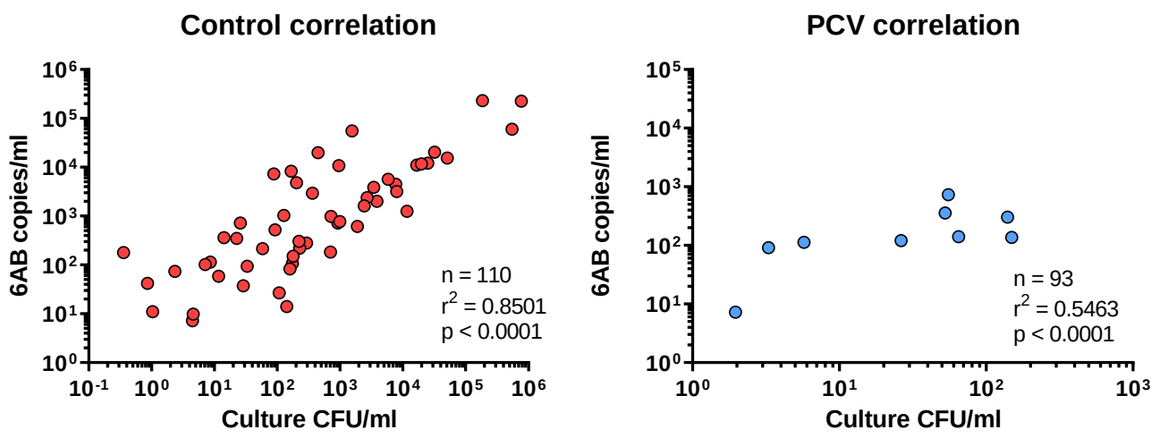
We evaluated 193 samples from 90 volunteers and showed that PCV conferred 83% protection against experimental pneumococcal colonisation by classical culture and 29% protection by molecular methods

Table 1. Comparison of numbers of colonised volunteers by detection method, study day and study arm

	Classical Culture No. Colonised/Total No. (%)		*lytA/cpsA* multiplex qPCR No. Colonised/Total No. (%)	
	PCV	Control	PCV	Control
D2	2/38 (5)	18/39 (46)	11/38 (29)	21/39 (54)
D7	4/43 (9)	18/42 (43)	16/43 (37)	23/41 (56)
D14	1/9 (11)	18/23 (79)	2/9 (22)	17/23 (74)
Any Day	**4/45 (9)**	**23/45 (51)**	**22/45 (49)**	**31/45 (69)**
Risk Ratio (p-value)	0.17 (0.0005)		0.71 (0.06)	

Definition of abbreviations: PCV = pneumococcal conjugate vaccine; NW = nasal wash

Correlation between densities calculated by classical culture and molecular methods

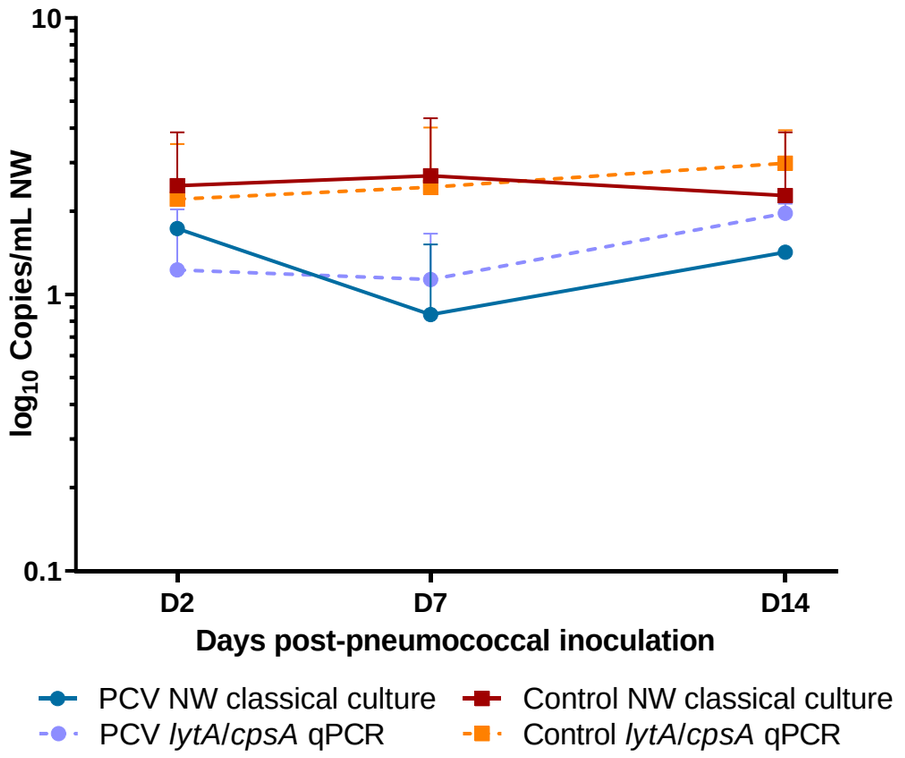


Colonisation densities by molecular methods

Colonisation densities were significantly lower in volunteers vaccinated with PCV compared to the control arm by both classical culture (p=0.03) and molecular methods (p<0.0001). 91% of samples positive by *lytA/cpsA* qPCR but not by classical culture had densities <30 DNA copies/ml

Table 2. Comparison of colonisation density of colonised volunteers by detection method, study day and study arm

	Classical Culture Log_{10} CFU/ml Mean ± SD		*lytA/cpsA* multiplex qPCR Log_{10} DNA copies/ml Mean ± SD	
	PCV	Control	PCV	Control
D2	1.73 ± 0.02	2.47 ± 1.39	1.22 ± 0.80	2.21 ± 1.29
D7	0.85 ± 0.67	2.70 ± 1.64	1.13 ± 0.52	2.44 ± 1.56
D14	1.42	2.28 ± 1.58	1.86 ± 0.16	2.98 ± 0.93



CONCLUSIONS

1. We showed, by using molecular methods instead of classical culture, that protection conferred by PCV vaccination against experimental colonisation reduces from 83% to 29%. This may indicate that the main protective mechanism of this vaccine is mediated by reduction of colonisation density, leading to a decreased risk of disease to vaccinated individuals as well as transmission resulting in the observed herd effects in vaccinated populations.

2. Studies assessing the impact of pneumococcal vaccines should allow for density measurements in their design.

References: 1. German, E. L. Solórzano, C. et al. Vaccine 37, (2019). **2.** Collins, A. M. et al. Am. J. Respir. Crit. Care Med. 192, 853–858 (2015). **3**. Carvalho, M. d. G. S. et al. J. Clin. Microbiol. 45, 2460–2466 (2007). **4**. Azzari, C. et al. PLoS One 5, e9282 (2010).

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