Antibody responses after a reduced dose schedule with the pneumococcal conjugate vaccine; Timing of the booster dose in the first or second year of life

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Introduction

Invasive pneumococcal disease (IPD) has the highest incidence rate in children less than 2 years of age but remains increased until 5 years of age. Several countries have implemented PCV7 vaccination programs for infants with 2 instead of 3 PCV7 injections before 6 months of age and with different timing of the booster dose in the second year of life. Delaying the booster dose possibly induces higher and sustained IgG antibody levels.

Aim

To compare IgG antibody responses in children after 2 primary PCV7 doses at 2 and 4 months of age followed by a booster dose at either 11 or at 24 months of age. Antibody levels were also compared with IgG levels after a first PCV7 vaccination at 24 months of age. Also the value of a booster dose at both 11 and 24 months was determined.

Methods

This study was part of the MINOES trial (ISRCTN25571720). PCV-7 schedules and age of blood sampling are described below. Serum for antipneumococcal vaccine serotype IgG antibody levels was obtained from 80 children in each group. and determined by double absorption ELISA (CPS and 22F-PS). Statistical differences in IgG GMC value's (Figure 1 and 2) were assessed by unpaired t test (log transformed). All p-values are 2-sided.

PCV-7 Schedules (months)	2	4	11	12	24	25
2 doses	٥	0		6		
2 doses + booster 11 months	٥	٥	0	۵		
2 doses + booster 24 months	0	0			🍐 /۞	۵
2 doses + 11+24 months	٥	٥	٥		⊘ ♦	۲
1 dose at 24 months					⊘	۵

Results

Figure 1: After 2 primary doses, higher IgG antibody levels after a PCV-7 booster dose scheduled at 24 months of age in comparison to a 11 month booster dose



#p<0.05: Post-booster values 11 vs. 24 months.</p>

Figure 2: No additional benefit of extra booster at 11 months when comparing PCV-7 adminstration at 2, 4, 11 and 24 months with a 2, 4 and 24 months schedule (GMC antibody responses)



Post-booster 24 months

Pre-booster 24 months; previous booster 11 months

Post-booster 24 months; previous booster 11 months

Table 1: Antibody responses pre- and post-PCV-7 as primary dose in infants at 24 months of age (GMC; µg/ml)

	GMC µg/ml (95% Cl)		% infants GMC	0.35 µg/ml	
Serotype	Pre-PCV7	Post-PCV7	Pre-PCV7	Post-PCV7	
	n = 77	n = 79	n = 77	n = 79	
4	0.10 (0.08-0.11)	2,65 (2.01-2.96)	7.8%	98.7%	
6B	0.24 (0.19-0.28)	0,55 (0.42-0.70)	24.7%	63.3%	
9V	0.14 (0.10-0.17)	1,73 (1.42-2.03)	18.2%	96.2%	
14	0.41 (0,31-0,50)	2,50 (1.87-3.30)	48.1%	96.2%	
18C	0.11 (0,09-0,14)	2,61 (2.15-3.08)	10.4%	98.7%	
19F	0.91 (0,74-1,10)	1,92 (1.61-2.28)	85.7%	98.7%	
23F	0.16 (0,13-0,19)	0,70 (0.52-0.94)	16.9%	60.8%	

Conclusions

>After 2 primary doses, a booster vaccination at 24 months of age resulted in significantly higher GMC IgG antibody levels for all seven vaccine serotypes compared to post-booster antibody levels at the 11 months (Figure 1)

Comparing the schedule 2, 4, 11 and 24 months with 2, 4 and 24 months, the extra booster at 11 months failed to contribute to postbooster antibody levels at 24 months of age (Figure 2)

After a first PVC-7 vaccination at 24 months of age, all GMC IgG levels to the 7 vaccine serotypes reach serum levels $\geq 0.35 \,\mu$ g/ml for >95% of the children, except for the low immunogenic serotypes 6B and 23F (Table 1)

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