A Non-Inferiority Trial, Comparing Two-Dose Priming with the 10-Valent Pneumococcal Conjugate Vaccine at 6 and 10 Weeks with 6 and 14 Weeks in Nepali Children

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INTRODUCTION

Nepal introduced PCV10 in 2015 using a unique 3-dose schedule (4-week interval between 2-priming doses; 6 weeks/10 weeks/9 months). A previous Nepal study[1] demonstrated better and longer-lasting immunity after the third dose of a 2p+1 schedule (8-week interval between priming doses; 6w/14w/9m) than after the 3p+0 schedule (6w/10w/14 w) used in most GAVI countries; both schedules are now WHO-recommended. However, as injectable polio was also being added to Nepal's EPI schedule at 14 weeks, it was felt that going from one injection to three would be programmatically difficult for both parents and vaccinators, so a 6w/10w+9m schedule was chosen.

A single centre open-label, parallel-group, randomised, controlled trial was undertaken to determine whether the 6w/10w schedule is non-inferior to the 6w/14w priming schedule, each followed by a booster dose at 9 months of age (9m).

METHODS

- From August 2015 to April 2016, 304 healthy Nepali children were randomised to 2 groups of 152 participants each.
- Blood was collected one month after the PCV10 second priming dose, and pre-post boost at 9 and 10 months of age.
- Serotype-specific antibody concentrations were determined by ELISA using 22F adsorption at a WHO pneumococcal serology reference laboratory.

RESULTS

IgG Antibody Titres ≥ 0.35µg/mL:

- At 9m, the 6w/10w schedule was non-inferior to the 6w/14w schedule for serotypes 5, 9V, 14, and 19F, but not for serotypes 1, 4, 6B, 7F, 18C, and 23F.
- One month after the second dose, the proportion of children above the protective threshold for the 6w/10w schedule was significantly different to the 6w/14w schedule, for serotypes 1, 6B, 18C and 23F.
- One month after the booster dose at 9 months, there was no difference between the two groups for any of the serotypes.

Proportion of IgG above protective threshold

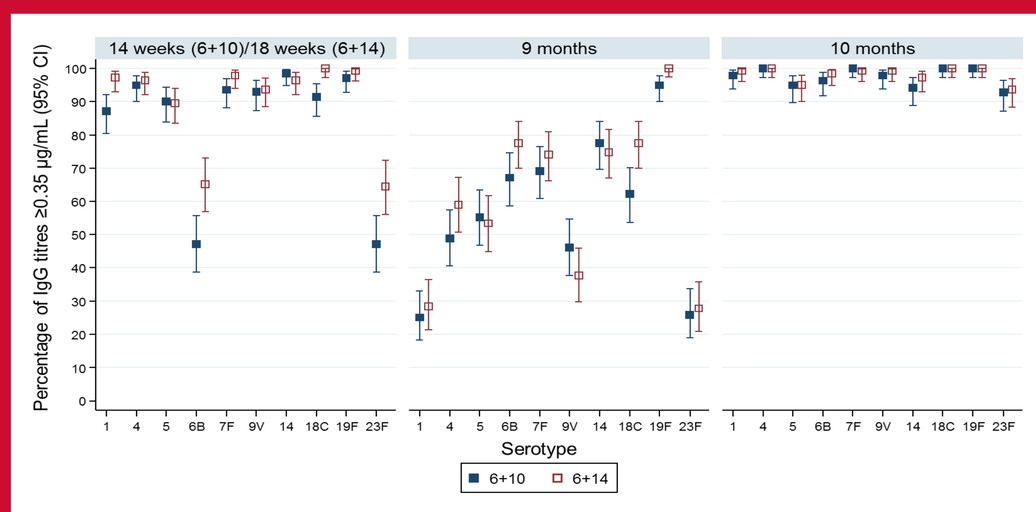

Figure 1: The proportion above the protective threshold for some serotypes is statistically different at 1 month after the second dose. There is no difference at 10 months after the 9-month booster.

Geometric mean IgG concentrations

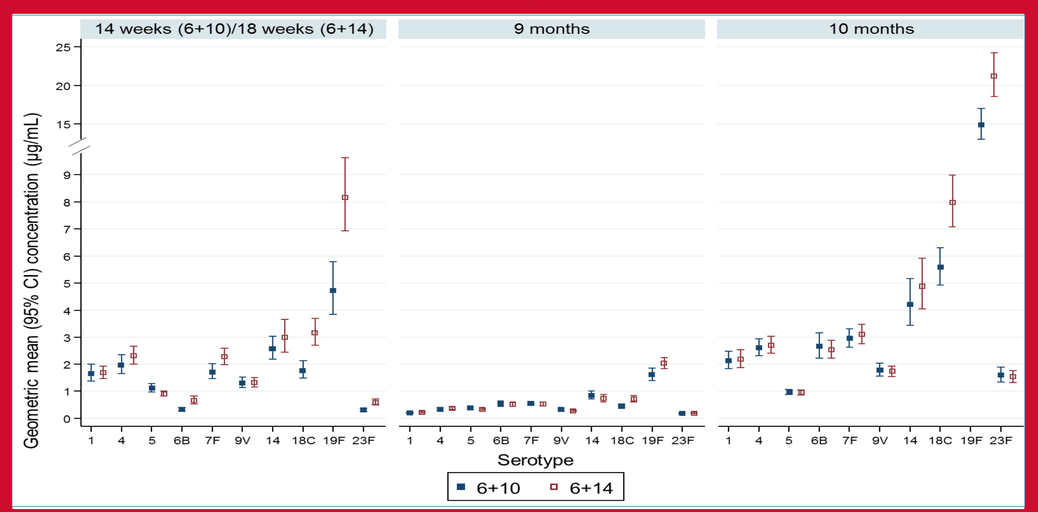

Figure 2: Geometric Mean antibody concentrations show that the 6/14 week schedule is better than 6/10 week schedule for 18C and 19F serotypes. These differences are probably not clinically important, especially after the 9-month booster.

Geometric Mean Antibody Concentrations:

- At both 9m and 10m, GMCs for the 6w/10w schedule were significantly different to the 6w/14w schedule for serotypes 18C and 19F but not for serotypes 1, 4, 5, 6B, 7F, 9V, 14 and 23F.

CONCLUSION

- One month after the second dose and at 9 months, the 6w/14w schedule is more immunogenic for some serotypes.
- After the 9 month booster, at 10 months the 6w/10w/9m and 6w/14w/9m schedules are comparably immunogenic.
- The 6w/14w/9m schedule is preferred where delivery logistics allow.

REFERENCE

1Hamaluba M, Kandasamy R, Gurung M, Thorson S, Pollard AJ et al. Comparison of two-dose priming plus 9-month booster with a standard three-dose priming schedule for a ten-valent pneumococcal conjugate vaccine in Nepalese infants: a randomised, controlled, open-label, non-inferiority trial: (2015) The Lancet Infectious Diseases, Volume 15 , Issue 4 , 405 - 414

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