

TITLE: COMPARISON OF THE EFFICACY OF A PROTEIN VACCINE AND A CONJUGATE VACCINE IN THE CONTROL OF PNEUMOCOCCAL CO-COLONIZATION IN MICE

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ABSTRACT:

Streptococcus pneumoniae is an opportunistic pathogen that colonizes the human upper respiratory system and can cause a range of infections, such as otitis media and pneumonia. The currently used conjugate vaccines cover only up to 13 (PCV13) of the 98 described pneumococcal serotypes. This vaccine is effective against invasive disease caused by vaccine serotypes (VT); however, its use has led to increase both in colonization and disease caused by non-vaccine serotypes (NVT). Alternative strategies to broaden coverage include the use of protein antigens, such as Pneumococcal surface protein A (PspA). PspA shows some diversity and is classified in 6 clades. The aim of this work is to compare the efficacy of PCV13 and PspA in a model of nasopharyngeal co-colonization of mice, mimicking the common situation of colonization with more than one pneumococcal isolate in children. We established two co-colonization models with a mixture of one VT strain and one NVT strain: a. TIGR4 (serotype 4, VT, PspA3) + 4431/119 (serogroup 33, NVT, PspA1) and b. 368/06 (serotype 23F, VT, PspA2) + 237/53 (serotype 15B/C, NVT, PspA4). Mice were immunized intranasally with recombinant PspA1 and PspA4 using wP (whole cell pertussis vaccine) as adjuvant (PspA1 + PspA4 + wP) and PCV13 was given subcutaneously. In the first co-colonization model, immunization with PCV13 led to a decrease in TIGR4 (VT, PspA3) and a small increase in 4431/119 (NVT, PspA1). Immunization only with the adjuvant wP led to a non-specific reduction of both strains. Immunization with protein led to statistically lower loads of both strains compared to saline, but only 4431/119 showed reduction compared to the group inoculated with adjuvant. In the second co-colonization model, no differences in bacterial loads were observed for animals immunized with PCV13 and challenged with 368/06 (VT, PspA2) + 237/53 (NVT, PspA4). The non-specific effect of wP was observed again for both strains. Immunization with protein led to statistically lower loads of both strains compared to saline, but only 368/06 (VT, PspA2) showed reduction compared to the group inoculated with adjuvant. PCV13 thus led to a reduction in loads of serotype 4, but not serotype 23F, both VT strains. Immunization with PspA1 + PspA4 + wP led to lower loads of strains expressing PspA1 and PspA2 compared to wP, but failed to protect against strains expressing PspA3 and PspA4, though reduction compared to saline was observed for all strains.

Keywords: *Streptococcus pneumoniae*, PspA, PCV13, co-colonization

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