Vaccine Reports 6 (2016) 36–43

Contents lists available at ScienceDirect

Vaccine Reports

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

Original Article

Limited impact of neonatal or early infant schedules of 7-valent pneumococcal conjugate vaccination on nasopharyngeal carriage of *Streptococcus pneumoniae* in Papua New Guinean children: A randomized controlled trial

Celestine Aho [a,b], Audrey Michael [a,1], Mition Yoannes [a], Andrew Greenhill [a,c,d], Peter Jacoby [d], John Reeder [a,e], William Pomat [a,d], Gerard Saleu [a], Pioto Namuigi [a,1], Suparat Phuanukoonnon [a,f], Heidi Smith-Vaughan [b], Amanda J. Leach [b], Peter Richmond [g], Deborah Lehmann [d,*], for the Neonatal Pneumococcal Conjugate Vaccine Trial Study Team [2]

[a] *Papua New Guinea Institute of Medical Research, PO Box 60, Goroka 441 EHP, Papua New Guinea*
[b] *Child Health Division, Menzies School of Health Research, PO Box 41096, Casuarina, Northern Territory 0811, Australia*
[c] *School of Applied and Biomedical Sciences, Federation University, Churchill, Victoria, Australia*
[d] *Telethon Kids Institute, The University of Western Australia, Perth, PO Box 855, West Perth, WA 6872, Australia*
[e] *Burnet Institute, 85 Commercial Road, Melbourne, Vic 3004, Australia*
[f] *The Walter and Eliza Hall Institute, 1G Royal Parade, Parkville, Vic 3052, Australia*
[g] *School of Paediatrics and Child Health, The University of Western Australia, Perth Western Australia, Australia*

ARTICLE INFO

Article history:
Received 20 April 2016
Revised 5 August 2016
Accepted 5 August 2016

Keywords:
Papua New Guinea
Streptococcus pneumoniae
Carriage
7-Valent pneumococcal conjugate vaccine
Pneumococcal serotype
Neonate

ABSTRACT

Streptococcus pneumoniae is a leading cause of pneumonia, the most common cause of childhood death. Papua New Guinean children experience high rates of nasopharyngeal pneumococcal colonization within weeks of birth, predisposing them to pneumococcal disease. In a trial to determine the safety and immunogenicity of early infant vaccination with 7-valent pneumococcal conjugate vaccine (7vPCV), we investigated the impact of early schedules on pneumococcal carriage.

Infants were randomized at birth to receive 7vPCV in a 0–1–2-month (n = 101) or a 1–2–3-month (n = 105) schedule or no 7vPCV (n = 106). All children received 23-valent pneumococcal polysaccharide vaccine at age 9 months. We cultured nasopharyngeal swabs (NPS) collected at ages 1, 2, 3, 4 weeks and 3, 9, 18 months, and middle ear discharge if present. Pneumococcal serotypes were identified by the Quellung reaction.

A total of 1761 NPS were cultured. The prevalence of pneumococcal carriage was 22% at 1 week of age, rising to 80% by age 3 months and remained >70% thereafter, with high-density carriage in 42% of pneumococcus-positive samples. We identified 63 different serotypes; 43% of isolates from controls were 13vPCV serotypes. There were no significant differences in 7vPCV serotype carriage between 7vPCV recipients and controls at any age (22% vs. 31% at 9 months, p = 0.2). At age 9 months the prevalence of non-7vPCV carriage was 17% higher in 7vPCV recipients (48%) than in controls (25%, p = 0.02). More non-7vPCV serotypes were isolated from ear discharge in 16 7vPCV recipients than from 4 controls (48% vs. 25%, p = 0.13).

The limited impact of neonatal or accelerated infant 7vPCV schedules on vaccine serotype carriage is probably due to the early onset of dense carriage of a broad range of pneumococcal serotypes. While serotype-independent pneumococcal vaccines are needed in high-risk populations, the underlying environmental factors and sources of infection must be investigated.

http://clinicaltrials.gov/ct2/show/NCT00219401.

© 2016 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

* Corresponding author.
E-mail addresses: Celestine.Aho@cdu.edu.au (C. Aho), Mition.yoannes@pngimr.org.pg (M. Yoannes), andrew.greenhill@federation.edu.au (A. Greenhill), peter.jacoby@telethonkids.org.au (P. Jacoby), reederj@who.int (J. Reeder), William.pomat@pngimr.org.pg (W. Pomat), Gerard.saleu@pngimr.org.pg (G. Saleu), suparatp@hotmail.com (S. Phuanukoonnon), Heidi.Smith-Vaughan@menzies.edu.au (H. Smith-Vaughan), Amanda.Leach@menzies.edu.au (A.J. Leach), Peter.richmond@uwa.edu.au (P. Richmond), Deborah.Lehmann@telethonkids.org.au (D. Lehmann).

[1] Deceased.

[2] Membership of the Neonatal Pneumococcal Conjugate Vaccine Trial Study Team is provided in Acknowledgements.

http://dx.doi.org/10.1016/j.vacrep.2016.08.002
1879-4378/© 2016 The Author(s). Published by Elsevier Ltd.
This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

1. Introduction

Pneumonia is the most common cause of death in children worldwide [1]. *Streptococcus pneumoniae* (the pneumococcus) is a major cause of pneumonia as well as other invasive diseases such as meningitis and bacteraemia. It is also responsible for non-invasive diseases such as otitis media (OM) which can result in hearing loss [2]. Nasopharyngeal carriage of *S. pneumoniae* predisposes individuals to pneumococcal diseases; early carriage in infants is associated with increased risk of OM and is found in populations with a high incidence of invasive pneumococcal disease (IPD) [3,4]. In the highlands of Papua New Guinea (PNG), colonization of the nasopharynx starts within weeks of birth, with all infants acquiring *S. pneumoniae* by 3 months of age and high carriage rates being maintained throughout childhood [4–6]. Pneumonia remains the most common cause of death and reason for hospitalization in childhood in PNG [7,8]. Mortality due to acute lower respiratory infections (ALRI), in particular pneumonia, was reported in 1999 to be highest in the first year of life, with 56% of deaths in children under the age of five years occurring before six months of age [9].

Pneumococcal conjugate vaccines (PCVs) have been used to combat pneumococcal disease in infants. A protein carrier is linked to an otherwise T cell-independent polysaccharide antigen to evoke an immunological response and enhance long-term memory to serotypes included in the vaccines. The introduction and widespread use of PCVs in first world countries has resulted in a significant decline in nasopharyngeal carriage and IPDs caused by vaccine serotypes in children under the age of 2 years. PCVs also indirectly protect unvaccinated people through herd immunity [10–12]. Encouraging results have also been seen in third world settings where PCVs have been trialled [13,14]. PCV given at ages 6, 10 and 14 weeks in third world countries and 2, 4 and 6 months with a booster in the second year of life in first world countries are immunogenic and reduce nasopharyngeal carriage of pneumococcal serotypes included in PCVs [10,15]. In addition, a pneumococcal polysaccharide vaccine has previously been shown to reduce pneumonia mortality in PNG children when given between the ages of 6 months and 5 years [16]. However, in populations where carriage occurs within weeks of birth and where morbidity and mortality due to ALRI are highest in the first 6 months of life, interventions at a very young age are necessary. Hence, a trial evaluating an accelerated schedule including a neonatal PCV dose was carried out to assess the safety and immunogenicity of the seven-valent PCV (7vPCV) in children living in the Asaro Valley, Eastern Highlands Province, PNG. We have previously reported that neonatal and early infant immunization with 7vPCV is safe and immunogenic [17]. We now aim to describe the effect of 7vPCV on nasopharyngeal carriage of pneumococci and pneumococcal serotypes when given either in a 0–1–2 or 1–2–3-month schedule. We also look at the effect of 7vPCV on pneumococci isolated from ear discharge swabs of children with tympanic membrane perforation (TMP) due to OM.

2. Methods

A detailed description of the study site and population, process of recruitment, assent and consent, enrolment, randomisation method, allocation concealment, study staff and participant blinding, laboratory staff blinding, and participant characteristics by allocated group, immunization and follow-up for primary outcomes are reported elsewhere [17,18]. A brief overview is given below.

2.1. Study design

The neonatal pneumococcal conjugate vaccine trial was carried out between 2005 and 2009. It was an open-label randomized controlled trial of 7vPCV (Wyeth/Pfizer; serotypes 4, 6B, 9V, 14, 18C, 19F & 23F) given at the ages of 0, 1 and 2 months (neonatal group) or at 1, 2 and 3 months (infant group) and a group that received no 7vPCV (control group). Study design and procedures are reported elsewhere [18]. All the children received other vaccinations according to the PNG Expanded Programme on Immunization [18,19] and 23-valent pneumococcal polysaccharide vaccine (PPV, Merck & Co, Inc; serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F and 33F) was given at 9 months of age. Participants were followed up to the age of 18 months.

Participant recruitment is reported in Pomat et al. [17]. Inclusion criteria for enrolment were: the intention to remain in the study area for at least 2 years, a birth weight > 2000 grams, no acute neonatal infection, no severe congenital abnormality, and born in Goroka General Hospital (GGH) or brought to GGH within 24 h of birth. Children of mothers known to be HIV-positive were excluded.

2.2. Nasopharyngeal swab collection

Infants were seen either at home or at the PNG Institute of Medical Research (PNGIMR) clinic at ages 1, 2, 3 and 4 weeks and 3, 9 and 18 months. Nasopharyngeal swabs (NPS, rayon-tipped swabs with metal shaft. Medical Wire and Equipment, Wiltshire, England) were collected and processed according to WHO recommended procedures for pneumococcal carriage studies [20]. The swab was inserted into the nasopharynx until resistance was met and then rotated for five seconds. Immediately following collection, the swab was placed in 1 ml of skim milk tryptone glucose glycerol broth (STGGB) [20]. The swabs were kept cool in an insulated container with ice packs and taken to the PNGIMR bacteriology laboratory within 2 h and stored at −80 °C until processed.

Ear discharge swabs (Amies Copan, Interpath Services, Australia) were collected from children who had purulent ear discharge on examination. Ear discharge swabs were placed directly into 1 ml STGGB and transported and stored as for NPS.

2.3. Culture of nasopharyngeal swabs and ear swabs

Approximately 12% of NPS (235/1996) were lost following a freezer thaw (details in results section). The remaining NPS were cultured using standard bacteriological procedures [20] by laboratory staff blinded to PCV group. 10 μl aliquots of the NPS in STGGB were streaked onto horse blood agar, chocolate agar, gentamicin blood agar (5 μg/ml) and bacitracin chocolate agar (300 μg/ml). Plates were incubated overnight (18–24 h) at 37 °C in 5% CO_2-enriched atmosphere. Bacterial growth was quantified on the plate as follows: 0, no growth; 1, <20 bacterial colonies; 2, 20–50 bacterial colonies; 3, 50–100 bacterial colonies; 4, confluent growth on the primary streak of the plate; 5, confluent growth on the primary streak of the plate and colonies on the second streak; 6, confluent growth in the secondary zone and colonies in the third zone. A quantification code of 1–3 was considered low density while 4–6 was considered high density. Four suspected morphologically distinct individual colonies of pneumococci on the primary plate (α-haemolytic low convex, plateau or draughtsman-shaped colonies) were picked and tested for optochin (5 μg ethylhydrocupreine, Oxoid, Australia) sensitivity. A zone of growth around the optochin disc of ⩾14 mm diameter was considered

Download English Version:

https://daneshyari.com/en/article/2474432

Download Persian Version:

https://daneshyari.com/article/2474432

Daneshyari.com