Immunogenicity of alternative and reduced immunization schedules using the thirteen-valent polysaccharide conjugate vaccine against infection with Streptococcus pneumoniae

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To assess the effect of alternative and reduced doses pneumococcal vaccination schedules using the 13-valent pneumococcal conjugate vaccine (PCV13, Wyeth) on the development of antibody titers directed against the different serotypes of pneumococci...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON35410

Source
ToetsingOnline

Brief title
Pneumococcal vaccination: reduced and different schedule

Condition

- Bacterial infectious disorders

Synonym
pneumococcal infection, Streptococcus Pneumoniae

Research involving
Human

Sponsors and support

Primary sponsor: RIVM
Source(s) of monetary or material Support: Ministerie van VWS

Intervention

Keyword: immunization schedule, Prevenar-13®, Streptococcus pneumoniae

Outcome measures

Primary outcome

Assessing the optimal PCV vaccination schedule: To assess the effect of the use of pneumococcal vaccination schedules with alternative timing and reduction of the number of vaccination doses on the serological response directed against the different serotypes of pneumococci. This information will be used to investigate whether a different timing or reduction of the vaccination schedule will induce antibody responses that are equal to or better than those obtained by the currently used vaccination schedule.

For each vaccine group, differences in serotype specific antibody concentrations between different schedules will be analysed. The primary endpoints are the antibody concentrations against pneumococcal polysaccharides for each serotype at 12 months in the different study arms. GMCs and the degree of protection (the proportion with concentration > 0.35 µg/ml) will be determined.

Secondary outcome

Kinetics of the antibody titer: To assess the kinetics of the pneumococcal antibody titers, in particular in the interval between the last vaccination dose of the primairy series and the booster vaccination at 11 months. This

period coincides with the peak incidence of pneumococcal invasive disease. The antibody concentrations of the longitudinal samples of each child will be used to assess the kinetics.

Interference of vaccination with PCV on other vaccinations: To investigate the possible influence of the pneumococcal vaccination on the serological responses of the other vaccine components of the NIP which are administered simultaneously in the other limb (DTaP-IPV-Hib). For this the antibody concentrations (GMCs) directed to the other vaccine components of the NIP will be determined.

Study description

Background summary

In the Netherlands nationwide pneumococcal vaccination was introduced in June 2006, with a 4-dose schedule in which children receive their vaccinations at 2, 3, 4 and 11 months of age. The reduction of the current 4-dose schedule into a 3-dose pneumococcal vaccination schedule would result in a smaller burden for the children and would cause an annual reduction of approximately ¤ 8,000,000 in costs for the National Immunization Program (NIP). A reduced vaccination schedule might require different vaccination moments, at a later age when the immune system of the infant is better developed and results in a better spread over the child*s most vulnerable period (e.g. at 3 and 5 months). The Dutch Health Council (Gezondheidsraad) who advises the Minister of Health would like to see more information about shorter vaccination programmes so that these can be introduced, where possible, in the near future*. The vaccination study described in this protocol is in full agreement with the advice of the Health Council and also is proactive as it will be performed using the new 13-valent pneumococcal conjugate vaccine instead of the currently used 7-valent vaccine.

Study objective

To assess the effect of alternative and reduced doses pneumococcal vaccination schedules using the 13-valent pneumococcal conjugate vaccine (PCV13, Wyeth) on

the development of antibody titers directed against the different serotypes of pneumococci. As an alternative 3+1 schedule we will use vaccination at 2, 4, 6 and 11 months (*USA schedule*) and compare this with 3+1 schedule currently used in the Dutch national immunization program in which children receive vaccination at 2, 3, 4 and 11 months. To investigate the possibility to reduce the vaccination schedule from 3+1 to 2+1 we include schedules in which the PCV13 will be administered at 2, 4 and 11 months (*UK schedule*) and 3, 5 and 11 months of age (*Scandinavian schedule*).

Study design

A randomized controlled parallel group trial. Children are randomly assigned to 4 groups receiving PCV13 i) at 2, 3, 4 and 11 months of age, ii) at 2, 4, 6 and 11 months of age, iii) at 2, 4 and 11 months of age and iv) at 3, 5 and 11 months of age. Children of the study groups with the reduced schedules will be offered an extra vaccination at 24 months of age to ensure they receive the same number of vaccinations as the children receiving the current NIP vaccination.
During the study 4 blood samples are taken from each child enrolled in the study at 1 month post primairy series, 8 months of age, pre-booster (11 months of age) and one month post-booster (12 months of age). Besides the blood samples, questionnaires including questions concerning clinical manifestations of allergic reactions are completed. Adverse events and SAE*s are recorded in the CRF.

Intervention

See study design

Study burden and risks

All children receive vaccinations against S. pneumonia, which may result in some form of minor side effects. It is not expected that PCV13 will give more side effects than PCV7, which all children currently receive in the NIP.
Immune responses of children vaccinated in different vaccination schemes will be compared. This requires the drawing of 2 ml blood samples at various time points during and after the vaccination series. The burden and risk associated with the blood collection is low. The children may find the needle scary and experience the puncture as painful. A local anaesthetic (Emla® crème, Astra Zeneca) will be used to minimize pain. Blood collection could result in a small bruise at the location of injection, which will disappear within a few days.
A questionnaire will be used to relate immune functions to clinical manifestations of allergic reactions.
This study is designed to further improve pneumococcal vaccination in the current NIP. The only possible study population is the group that would normally participate in the NIP. All participating children will receive PCV13

vaccine that protects them against 6 more serotypes than the PCV7 vaccine currently given in the NIP. Half of the children enrolled in the study will receive only 3 doses of the PCV13 vaccine, one dose less than the number of doses used in the Dutch NIP in the first year of life. However, this 2+1 schedule, , is an accepted schedule in many other countries and is now also an accepted schedule according to the SPC of PCV7 and PCV13. Nevertheless, children of the study groups with the reduced schedules will be offered an extra vaccination at 24 months of age to ensure the same number of vaccination doses are administered as to children receiving the current NIP vaccination.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

• Infants in good general health, eligible to be vaccinated according to the Dutch national vaccination program. The same health criteria apply as used in well-baby clinics when a child

receives a vaccination, e.g. also children with small increases in temperature or cold are seen as children with normal health.
• The parents have to be willing and able to allow their child to participate in the trial according to the described procedures
• Presence of a signed informed consent in which the parent(s)/legally representative(s) have given written informed consent after receiving oral and written information (signature from one parent in case of an orphan, or single-parent family).

Exclusion criteria

Any of the following criteria will exclude a volunteer from participation, at start of the study:
• Children elegible for the Hepatitis B vaccination
• Previous Prevenar and DTaP-IPV-Hib vaccination
• Present evidence of serious disease(s) demanding immunosuppressive medical treatment, like cytostatics and prednisolons, that might interfere with the results of the study within 3 months
• Any known primary or secondary immunodeficiency
• Vaccination with any vaccine other than those used in the RVP within a month before the blood sampling
• Bleeding disorders
• Premature birth (<37 weeks);Delay criteria
• In case of fever (>38.5 oC) the vaccination will be postponed
• In case a child is having fever (>38 oC) within 2 days before blood sampling which can interfere with the cellular immune responses at that time, another appointment for blood sampling will be made

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-06-2010
Enrollment:	400
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Prevenar-13®

Ethics review

Approved WMO Date:	24-03-2010
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-04-2010
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-07-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2009-014315-12-NL
CCMO	NL28918.000.09