Development of cellular immune response after infant pneumococcal conjugate vaccinations

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Primary objectiveTo determine the development of the cellular immune response (plasma B cells and memory B-cells), immediately before and after the booster of the 3+1 Prevenar® vaccination schedule at 11 months of age and before and after the...

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

Summary

ID

NL-OMON32887

Source
ToetsingOnline

Brief title
Pneumococcal cellular immune response

Condition

- Bacterial infectious disorders

Synonym
Immunogenicity, memory

Research involving
Human

Sponsors and support

Primary sponsor: Nederlands Vaccin Instituut
Source(s) of monetary or material Support: Ministerie van VWS

Intervention

Keyword: Immune response, Memory, Pneumococcal disease, Prevenar®

Outcome measures

Primary outcome

• Cellular immunogenicity (plasmacells and memory B-cells frequencies)

Secondary outcome

• Geometric mean titres (GMT)

• Avidity

• Opsonophagocytoses

Study description

Background summary

Prevenar®, a seven-valent pneumococcal conjugate vaccine has been registered for use in a so-called 3+1 vaccination schedule consisting of a three dose primary series followed by a booster vaccination. It has been introduced in the Dutch National Immunization Program in April 2006 for vaccination at 2, 3, 4 and 11 months of age.
Prevenar vaccination provides immediate protection against pneumoccocal related diseases through the induction of functional antibodies, which however only have a short half-life indicating the need for a memory response. Both the induction and maintenance of functional serum antibody titres have a cellular basis which is still poorly understood.
In general, antigens trigger naïve B-cells to expand and differentiate into two types of affinity matured B-cells: antibody secreting plasma B cells and memory B-cells. Since plasma cells are unlikely to persist for more than 6-8 weeks (Gourley TS et al, 2004) maintenance of steady state antibody levels over periods of years requires a continuous low level of differentiation of memory B cells into plasma cells. Factors such as recurrent antigen exposure such as through carriage might be involved in this process.
Prevenar is thought to induce immediate protection through stimulation of antibody production by polysaccharide specific plasma B cells, sustained protection is conferred by a memory B cell pool which induces an accelerated increase in antibody titres during secondary immune responses seen after re-infection or boosting.

An improved understanding of the immunobiology of the B-cell response to conjugate vaccines, such as Prevenar, is essential to develop immunization strategies that provide sustained protection.

Study objective

Primary objective
To determine the development of the cellular immune response (plasma B cells and memory B-cells), immediately before and after the booster of the 3+1 Prevenar® vaccination schedule at 11 months of age and before and after the challenge vaccination at 24 months of age

Secondary objective
To determine development of the immune response by looking at antibody concentrations, avidity and opsonophagocytoses immediately before and after the booster of the 3+1 Prevenar® vaccination schedule at 11 months of age and before and after the challenge vaccination at 24 months of age

Study design

Parallel group trial

Intervention

Group 4 receives a single challenge vaccination with Prevenar® vaccine

Study burden and risks

All children undergo one blood collection of 8 ml. The burden and risk associated with the blood collection is low. The children might find the needle scary and it might be painful (only for a few seconds). A local anaesthetic (Emla® crème, Astra Zeneca) may 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.
Children in group 4 (N=25) receive a challenge vaccination in order to stimulate the production of memory cells.
The Pneumococcal vaccination gives protection against invasive pneumococcal disease (IPD) caused by the 7 pneumococcal vaccine types. It is indicated for children aged 2-24 months. A vaccination at 24 months of age is a registered application, although not deemed necessary for protection once the children have received a 4 dose schedule (at 2, 3, 4 and 11 months of age). It is expected that the extra vaccination at 24 months of age will not cause any other side effects then the previous Prevenar® vaccinations.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Healthy children 11 or 24 months of age. The parents are willing and able to let their child participate in the trial according to the described procedures, with a a signed informed consent
The children have received (24 months old children) or will receive the Prevenar® vaccinations according to the 3+1 schedule as part of the Dutch NIP

Exclusion criteria

Previous vaccinations with Prevenar using a schedule that differs from the National Immunisation Program (3+1 schedule) or with other pneumoccocal vaccines.
Presence of a serious disease that can interfere with the results of the study

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-03-2009
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	29-07-2008
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-10-2008
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-01-2009
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	EUCTR2008-004489-23-NL
CCMO	NL24329.000.08