Maternal pertussis (Tdap) vaccination and its effects on the immune response of the newborn up to 12 months of age.

Published: 05-09-2013
Last updated: 15-05-2024

Primary objective;Confirm superiority of IgG antibody levels against pertussis toxin (Ptx), present in the acellular vaccines, in infants at the age of 3 months of mothers having received a pertussis vaccine during pregnancy versus infants of...

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

Summary

ID

NL-OMON44971

Source
ToetsingOnline

Brief title
Effects of maternal pertussis vaccination on infant immune response

Condition

- Bacterial infectious disorders

Synonym
Pertussis, Whooping Cough

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Boostrix, Maternal Vaccination, Pertussis

Outcome measures

Primary outcome

- Serum IgG antibody levels against pertussis vaccine antigen Ptx at 3 months of age, immediately before the start of infant vaccination

Secondary outcome

- Serum IgG antibody levels against pertussis vaccine antigens Ptx, FHA and Prn of the newborns at birth and at the infants age of 2, 3, 6, 11, 12, 24, 46 and 47 months
- Serum IgA antibody levels against pertussis vaccine antigens Ptx, FHA and Prn of the new-borns at birth and at infants age of 2, 3, 6, 11, 12, 24, 46 and 47 months
- Serum IgG antibody levels against tetanus (T) and diphtheria (D) to assess influence of maternal antibodies on the response to D and T vaccination of the new-borns at birth and at infants age of 2, 3, 6, 11, 12, 24, 46 and 47 months
- Serum IgG antibody levels against other concomitantly administered vaccine components Hib, HepB and pneumococcal serotypes (PCV10) of the new-borns at birth and at infants age of 2, 3, 6, 11 and 12 months
- Serum IgG antibody levels against pertussis vaccine antigens Ptx, FHA and Prn of the mothers, pre-vaccination, immediately postpartum and at 6, 12, 24 en 47 months after birth
- Frequency of local and systemic reactions after Tdap vaccination during pregnancy

- Frequency of pertussis specific memory B-cells and plasma cells immediately before and 7-9 days after the booster dose at 11 months

- Frequency of pertussis specific memory B-cells and plasma cells immediately before and 28-35 days after the booster dose of around 4 years of age.

- Compare infants* pain response and maternal attitude to infant blood collection by heel stick and venipuncture.

- Compare IgA levels against pertussis antigens in breast milk of mothers of both groups taken at 7-10 days, 3 months and 6 months after giving birth

Study description

Background summary

Pertussis, *Whooping cough* caused by the Bordetella pertussis bacterium, is a highly contagious potentially life-threatening respiratory illness especially in infants less than 6 months of age. Recently there has been a considerable increase in pertussis activity with a sharp increase in incidence rate in infants < 2months of age who are too young to be protected through routine vaccination but with the highest risk of complications and death. A possible alternative way to protect these very young infants is by indirect protection, either through a cocooning strategy, i.e. vaccinating primary caregivers of new-borns, or by passive transfer of maternal antibodies induced by maternal vaccination. The purpose of this trial is to evaluate the possibility to provide initial immunological protection of newborn babies against pertussis infection by passively acquired maternal IgGs after vaccination of pregnant women. Pregnant woman will receive a single dose of a combination vaccine including reduced dose acellular pertussis, tetanus toxoid and reduced dose diphtheria toxoid (Tdap) between week 30 and 32 of pregnancy. The control group will consist of pregnant women who will be vaccinated with the same Tdap vaccine postpartum. All infants, born of pregnant women of both groups, will then be vaccinated with the routine vaccines of the national immunisation program (NIP) DtaP-IPV-Hib-Hep and PCV10 at the age of 3, 5 and 11 months instead of the standard schedule of 2, 3, 4, and 11 months. Experience in other countries and our own research has shown that vaccinations at age 3 and 5 months, followed by a booster dose will result in equal clinical effectiveness

in protection against Hib, pneumococcus, diphtheria, tetanus and polio compared with a schedule which starts at 2 months of age. Infants will probably, up to 3 months of age, be protected through the presence of maternal pertussis antibodies (group 1) or by reducing the risk that new-borns will be infected by their parents by vaccinating their mother and partner or other primary caregivers (cocooning strategy, group 2). In this way the total number of vaccines each child gets can be reduced.

Study objective

Primary objective;
Confirm superiority of IgG antibody levels against pertussis toxin (Ptx), present in the acellular vaccines, in infants at the age of 3 months of mothers having received a pertussis vaccine during pregnancy versus infants of mothers who have been vaccinated postpartum.

Secondary objectives:
- Determine the effect of the presence of maternal antibodies in the infant on the infant's immune response to active immunization with pertussis vaccine
- Compare serum IgA levels against pertussis antigens of infants of both groups at the age of 2, 3, 6, 11, 12, 24, 46 en 47 months
- Determine the rate of maternal antibody decline in infants between birth and at 2 and 3 months of age before the first infant pertussis vaccination
- Determine levels of pertussis IgG antibodies transferred from the mother to the neonate relative to the interval from immunization to delivery, if possible depending on the variation in interval;
- Determine whether maternal immunization during pregnancy interferes with active antibody production following routine DTaP-IPV-Hib-Hep and PCV10 vaccination in infants at 3, 6, 11, 12, 24, 46 en 47 months of age
- Assess cellular immune response (Plasma B cells and memory B cells) immediately before and 7-9 days after the booster dose at 11-months of age
- Assess cellular immune response (Plasma B cells and memory B cells) immediately before and 28-35 days after the booster dose of around 4 years of age
- Safety evaluation after Boostrix (Tdap) vaccination during pregnancy
- Assess pertussis IgG antibody levels in mothers of both groups, pre-vaccination, at delivery (=pre-vaccination for control group) and at 6, 12, 24 and 47 months post-delivery;
- Compare IgA levels against pertussis antigens in breast milk of both groups at the infants age of 7-10 days and 3 and 6 months of age
- Compare infants pain response and maternal response to infant blood collection by heel stick and venipuncture

Study design

Randomised, controlled intervention trial

Intervention

Pregnant woman in group 1 will receives a single dose of Boostrix vaccine between week 30 and 32 of pregnancy and pregnant woman in group 2 will receive a single dose of Boostrix vaccine postpartum.
All partners or other caregivers will receive a single dose of Boostrix within 28 hours after birth.

Study burden and risks

Available data on the use of Tdap in pregnant women does not suggest any elevated frequency or unusual patterns of adverse events in pregnant women who received Tdap.

Group 1a and 2a; 7 heel/finger stick blood collections of 250 µl will be performed, the 11 months sample will be taken from the 4 ml sample.
Group 1b and 2b: 8 heel/finger stick blood collections of 250 µl will be performed.
The burden and risk is considered low.
One cord blood sample will be collected from all participating infants at birth.

One 8 ml blood sample will be collected from all infants, either immediately before vaccination at the age of 11 months or 7-9 days after the 11 months of age vaccination.
Optional: One 10 ml blood sample will be collected from infants, either immediately before vaccination at the age of 4 years or 28-35 days after vaccination of around 4 years of age. The burden and risk is considered low. It might be painful but only for a few seconds. Blood collection could result in a small bruise at the needle stick location, which will disappear within a few days.

To reduce the burden of 11-12 visits, home visits will be performed.

Mothers will be asked to collect 10 ml of breastmilk at 3 timepoints during the studie
The burden and risk is considered low.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

* Pregnant women 18-40 years of age ;* Women with a low risk of pregnancy complications as assessed by a midwife/obstetrician/gynaecologist with a normal 20 weeks ultrasound of the fetus;* Women who are willing to adhere to the protocol and perform all planned visits and sample collections for themselves and their newborn child;* Parents have to be willing to have their infant vaccinated with the hexavalent (DaKTP-Hib-Hep) vaccine at 3, 5 and 11 months of age according to the described procedures;* Presence of a signed informed consent

Exclusion criteria

Exclusion criteria for (pregnant) woman:
- History of having received a pertussis vaccination in the past 5 years
- History of having received a TD containing vaccine in the past 2 years
- Known or suspected serious underlying condition that can interfere with the results of the study such as but not limited to cancer, autoimmune disease, immunodeficiency, seizure disorder or significant psychiatric illness
- Receipt of any high-dose (* 20 mg of prednisone daily or equivalent) daily corticosteroids

(inhaled steroids are acceptable) within 2 weeks of study entry
- Receipt of other immune modulating medication, for instance biologicals
- Receipt of blood products or immunoglobulin, within three months of study entry (Rhesus negative women who receive antirhesus (D)- immunoglobuline will not be excluded from the trial)
- Presence of bleeding disorder
- Having experienced a previous severe adverse reaction to any vaccine
- Receipt of any vaccine(s) within 2 weeks of study vaccine (except influenza vaccine which may be given concomitantly)
- History of febrile illness (>38.0*C orally) within the past 72 hours (immunization may be deferred) ;Exclusion criteria for partners or other primary caregivers:
- Having experienced a previous severe adverse reaction to any vaccine
- History of febrile illness (>38.0*C orally) within the past 72 hours (immunization may be deferred) ;Exclusion criteria for new-borns of participating mothers:
- Serious underlying medical condition that can interfere with the results of the study
- Premature infants born before 37 weeks gestational age

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):	29-12-2013
Enrollment:	348
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Boostrix
Product type:	Medicine
Brand name:	Infanrix hexa
Product type:	Medicine
Brand name:	Synflorix

Ethics review

Approved WMO Date:	05-09-2013
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	03-10-2013
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	08-07-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-08-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-04-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	30-04-2015
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-05-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-02-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	31-10-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-11-2017
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

ID: 22463
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2013-003090-98-NL
CCMO	NL45652.000.13
OMON	NL-OMON22463

Study results

Results posted: 14-09-2020

Actual enrolment: 353

First publication
01-01-1900

URL result
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