Premature infants and maternal pertussis immunization. Is second trimester vaccination beneficial?

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Our primary objective is to evaluate non-inferiority of anti-Pertussis Toxin (PT) IgG in term infants at 2m of age born of mothers having received a pertussis vaccine between 20-24w Gestational Age (GA) compared to a reference anti-PT IgG at 2m of...

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

Summary

ID

NL-OMON49737

Source
ToetsingOnline

Brief title
PIMPI: Premature Infants and Maternal Pertussis Immunization

Condition

- Bacterial infectious disorders

Synonym
pertussis, whooping cough

Research involving
Human

Sponsors and support

Primary sponsor: RIVM
Source(s) of monetary or material Support: ZonMW subsidie

Intervention

Keyword: immunization, pertussis, preterms, second trimester of pregnancy

Outcome measures

Primary outcome

Serum IgG antibody levels against vaccine antigen PT in preterm and term infants at 2 months of age, before start of infant vaccination.

Secondary outcome

- The IgG antibody concentration against pertussis toxin (PT), pertactin (Prn) filamentous hemagglutinin (FHA), tetanus and diphtheria in the mother at delivery.

- The IgG antibody concentration against PT, Prn, FHA, tetanus and diphtheria in the infant at birth (cord blood).

- The IgG antibody concentration against Prn, FHA, tetanus and diphtheria in the infant at 2m of age.

- The decay in IgG antibody concentration against PT, Prn, FHA, tetanus and diphtheria in infants from birth until 2 months of age.

- The ratio between maternal GMCs and infant GMCs at birth.

- Frequency of local and systemic adverse events occurring within 7 days after vaccination during pregnancy.

- Frequency of systemic events, occurring in the week before the maternal vaccination.

- Frequency of determinants of acceptance of 2nd trimester pertussis vaccination.

- Determinants of women*s attitude towards maternal pertussis vaccination

between 20-24w GA.

Study description

Background summary

Pertussis has resurged worldwide. Current epidemiology shows that very young infants do not profit from the currently used vaccination schedules and remain at highest risk for severe pertussis disease and even death. Therefore, a growing number of countries implemented 3rd trimester maternal pertussis vaccination. Through trans-placental transport of pertussis specific antibodies, infants are protected in the first months of life. Data have shown that this intervention is 91% effective in preventing pertussis in young infants and 95% effective in preventing death due to pertussis. However, data also show that preterm infants profit less from 3rd trimester pertussis vaccination, probably due to insufficient time for antibody transfer. At the same time, preterm infants are overrepresented in pertussis notifications and hospitalisations. Some countries have implemented 2nd trimester pertussis vaccination, with good immunogenicity data. In contrast, another study showed that 2nd trimester pertussis vaccination is less effective in preventing infant pertussis than 3rd trimester immunisation. Therefore, it is important to gain more insight into second trimester maternal pertussis vaccination. In the Netherlands, maternal pertussis vaccination will be implemented late 2019 and probably will be offered from 22 week gestational age onwards.

Study objective

Our primary objective is to evaluate non-inferiority of anti-Pertussis Toxin (PT) IgG in term infants at 2m of age born of mothers having received a pertussis vaccine between 20-24w Gestational Age (GA) compared to a reference anti-PT IgG at 2m of age in a historical control group of term infants born of mothers who were vaccinated between 30-32w GA. Likewise, we aim to assess non-inferiority of anti-PT IgG in preterm infants at 2m of age born of mothers having received a pertussis vaccine between 20-24w GA compared to the 20 IU/ml anti-PT IgG cut-off used in many immunogenicity studies.

Study design

We will set up a prospective cohort study of pregnant women with follow up of their infants up to 2 months of age. The study consists of two parts. The first part aims to study acceptance of 2nd trimester pertussis vaccination and the relation between determinants and actual behavior, i.e. acceptance of vaccination. Women who actually received a 2nd trimester pertussis vaccination will be asked to also participate in the second study part, i.e. the

immunogenicity part.

Intervention

Pregnant woman can choose to receive a single dose of Boostrix vaccine between week 20 and 24 of pregnancy

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.
One heel/finger stick blood collections of 100 µl will be performed in the mother after delivery and in the infant at 2m of age. The burden and risk is considered low. It might be painful but only for a few seconds.
One cord blood sample will be collected from all participating infants at birth.

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

1. 18 years or older , 2. Being pregnant , 3. Having an antenatal appointment with a midwife or obstetrician in the 1st trimester of pregnancy , 4. Signed informed consent , 5. Parents who are willing to adhere to the protocol and perform all planned visits and, sample collections for themselves and their newborn child (only relevant for the immunogenicity part

Exclusion criteria

1. All women with one or more missing inclusion criteria, 2. History of having received a pertussis containing vaccination in the past 2 years. , 3. History of having had pertussis disease in the past 5 years., 4. 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., 5. Receipt of any high-dose (>=20 mg of prednisone daily or equivalent) daily corticosteroids within 2 weeks of study entry (inhaled or other local steroids are acceptable) with exception of corticosteroids to enhance maturation of fetal lungs in case of imminent early delivery., 6. Receipt of other immune modulating medication, for instance biologicals., 7. Receipt of blood products or immunoglobulins, within three months of study entry, (Rhesus negative women who receive anti-rhesus (D)- immunoglobulin will not be, excluded from the study)., 8. Presence of bleeding disorder., 9. Having experienced a previous severe adverse reaction to any vaccine., 10. Receipt of any vaccine(s) within 2 weeks of study vaccine (except influenza, vaccine which may be given concomitantly).

Study design

Design

Study phase:	4
Study type:	Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	07-08-2019
Enrollment:	6750
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Boostrix

Ethics review

Approved WMO Date:	27-06-2019
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-07-2019
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-07-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-09-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	27-11-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-07-2021
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: 21026
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2018-002976-41-NL
CCMO	NL66966.000.18
OMON	NL-OMON21026