Pregnancy Exposure to TNF alpha inhibitors and Immunological effecT in infants

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Intra uterine exposure to anti-TNFα inhibitors influences the normal development of the immune system, leading to immunodeficiency and immune dysregulation, with the potential to cause short term and long-term morbidity. TNFα plays an important role...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON22495

Bron
Nationaal Trial Register

Verkorte titel
PETIT

Aandoening

immunodeficiency, inflammatory bowel disease

Ondersteuning

Primaire sponsor: haga ziekenhuis, den Haag
Overige ondersteuning: Dr CJ Vaillant fonds

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

In order to assess the effects of anti-TNFα on the development of adaptive and innate immunity, children exposed to anti-TNFα (with or without other immunosuppressive drugs) will be compared to children exposed to immunosuppressive drugs (but no anti-TNFα) to evaluate for differences in:
1) immunological markers in relation to anti TNFα level (immunophenotyping of T and B cell subsets (in particular memory B cells at 12 months), presence of hypogammaglobulinaemia at 12 months)
2) the frequency of infections

Toelichting onderzoek

Achtergrond van het onderzoek

Relapse of inflammatory bowel disease (IBD) activity during conception and pregnancy is associated with a negative pregnancy outcome; prematurity and low birth weight. Therefore, disease remission during this period is of utmost importance and it is advised to maintain drugs such as Anti- Tumor Necrosis Factor alpha (anti TNFα), thiopurines and 5-aminosalicylic acid. Most IBD drugs are considered of low risk during pregnancy, since no increase of congenital malformations has been reported so far. However the effects on the developing immune system, after intra-uterine exposure, remain unknown. Anti TNFα drugs are effectively transferred through the placenta resulting in high levels in the new-borns. It is known that live vaccines must be avoided until the levels of anti TNFα are undetectable, as there has been one report of an infant, who died after a BCG vaccination associated with exposure to anti-TNFα in utero. Since studies are scarce and most of the data were collected retrospectively, there is an urgent need for prospective studies focussing on the impact of exposure to biologicals, especially anti-TNFα, in utero on the development of the immune system and the potential risk of clinical complications.

Main aim of this prospective longitudinal observational study is to answer the following questions: Does intra uterine exposure to anti TNFα 1) change the developing adaptive and innate immune system 2) have persistent/long term effects on the immune system 3) lead to more frequent and/or more severe infections?
Infants with intrauterine exposure to anti-TNFα used for maternal IBD will be compared to children exposed to other immunosuppressive drugs and to healthy children. Infants will be clinically monitored and repeated immunological studies will be performed in order to assess their immune status and susceptibility to infections.

Results will be used to guide immunosuppressive strategies during pregnancy in women with IBD. If intra uterine exposure to anti TNFα does indeed lead to abnormalities in the development of the immune system, new follow-up strategies will be developed for the detection and treatment of potential long-term complications

Doel van het onderzoek

Intra uterine exposure to anti-TNFα inhibitors influences the normal development of the immune system, leading to immunodeficiency and immune dysregulation, with the potential to cause short term and long-term morbidity. TNFα plays an important role in both innate as adaptive immune system. We hypothesize that intra uterine exposure to anti-TNFα inhibitors will affect the immune system in multiple ways having both an effect when (high) concentrations are present during pregnancy as well as beyond the neonatal period- because of the long half-life of this biological-, which may further affect the developing immune system. A prolonged effect may even be present after anti-TNFα inhibitors are no longer detectable, due to epigenetic changes in immune cells.

Onderzoeksopzet

birth, age 3 months, age 5 months, age 12 months

Onderzoeksproduct en/of interventie

non applicable

Contactpersonen

Publiek

Haaglanden Medisch Centrum en ErasmusMC-Sophia kinderziekenhuis
Jantien Bolt-Wieringa

088 979 7900

Wetenschappelijk

Haaglanden Medisch Centrum en ErasmusMC-Sophia kinderziekenhuis
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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Infants with intra uterine exposure to anti-TNFα (with or without other immunosuppressive

drugs) for maternal IBD and infants with intrauterine exposed to other immunosuppressive drugs (but no anti-TNFα) for maternal IBD Parents must have sufficient understanding of the Dutch language and be able to give informed consent. Parents must own a smartphone in order to be able to use the InfectionApp.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Infants in which informed consent is not obtained.
Infants with a (possible) HIV infection, infants with an immunodeficiency as part of a known genetic or inherited disease.
Infants of mothers using certolizumab, golimumab or eternacept are excluded, because they are hardly present in the cohort of pregnant women with IBD. In addition, certolizumab hardly passes the placenta

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Toewijzing:	Niet-gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-11-2018
Aantal proefpersonen:	160
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	31-05-2019
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 54516
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL7773
CCMO	NL63910.098.17
OMON	NL-OMON54516

Resultaten