Pregnancy Exposure to TNF alpha inhibitors and Immunological effecT in infants

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON22495

Source
NTR

Brief title
PETIT

Health condition

immunodeficiency, inflammatory bowel disease

Sponsors and support

Primary sponsor: haga ziekenhuis, den Haag
Source(s) of monetary or material Support: Dr CJ Vaillant fonds

Intervention

Outcome measures

Primary outcome

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

Secondary outcome

1) Differences in other immunological markers (response to routine vaccinations (Tetanus, H Influenzae type B, Pertussis, pneumococcal conjugate vaccine), immunoglobulin levels, presence of hypogammaglobulinemia at birth, 3 and 5 months, proteomics) between children exposed to anti-TNFα (with or without other immunosuppressive drugs) and children exposed to immunosuppressive drugs (but no anti-TNFα)
In order to further 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) and to healthy children for differences in:
2) innate and adaptive immunity by measuring immunological markers in relation to anti TNFα level (immunophenotyping of T and B cell subsets, immunoglobulin levels, presence of hypogammaglobulinemia, response to routine vaccinations (Tetanus, H Influenzae type B, Pertussis, pneumococcal conjugate vaccine), proteomics)
3) the frequency of infections
4) persistent /long term effects on the immune system by detecting epigenetic changes in mononuclear cells

Study description

Background summary

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

Study objective

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.

Study design

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

Intervention

non applicable

Contacts

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Eligibility criteria

Inclusion criteria

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.

Exclusion criteria

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

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL
Recruitment status:	Recruiting
Start date (anticipated):	01-11-2018

Enrollment:	160
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	31-05-2019
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 54516
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

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

Study results