Hepatitis B vaccine efficacy in children exposed to anti-TNF in utero

Published: 14-04-2014
Last updated: 24-04-2024

Primary Objective: - Antibodies to the hepatitis B surface antigen (anti-HBs) levels 30 days after the last hepatitis B vaccine dose (11 months) in children from IBD mothers treated with anti-TNF compared to children from IBD mothers not treated...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON40615

Source
ToetsingOnline

Brief title
HEFFIC study

Condition

- Other condition
- Gastrointestinal inflammatory conditions
- Postpartum and puerperal disorders

Synonym
Crohn's disease, ulcerative colitis

Health condition

werkzaamheid hepatitis B vaccinatie

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Anti-TNF, Hepatitis B vaccine, Inflammatory Bowel Disease, Pregnancy

Outcome measures

Primary outcome

- Antibodies to the hepatitis B surface antigen (anti-HBs) 30 days after the

final HBV vaccination at 11 months

Secondary outcome

- (if applicable) anti-HBs levels 4 weeks after HBV booster vaccination in the

primary non-immune children

- Anti-TNF levels from the cord blood, and if required when the child is 3

months old, 6 months old and 12 months old.

- Maternal anti-TNF levels at delivery

Study description

Background summary

Biological agents like anti-TNF have revolutionized the treatment of Inflammatory Bowel Disease (IBD) by successfully achieving and maintaining remission (1). IBD typically affects people at a young childbearing age (2), therefore some IBD women will require biological therapy during pregnancy. Anti-TNF agents have been accepted as generally safe during pregnancy as they do not give rise to an increased risk of congenital abnormalities, preterm birth, low birth weight or miscarriages (3, 4), however there are several long term effects left unexplored.
Several studies have demonstrated anti-TNF to actively cross the placenta in the second and especially the third trimester of pregnancy (5-7). Consequently, children from anti-TNF treated mothers are born with clinically significant

serum levels of anti-TNF.
A shocking case-report in 2010 (8) describing a fatal case of disseminated BCG disease in a child born to a mother deliberately treated with anti-TNF during pregnancy, has led to the avoidance or delay of administering live attenuated vaccines in these children. However, the efficacy of other passive vaccines, like the hepatitis B (HBV) vaccine, is unknown in children of this specific group of patients.
There is evidence that the HBV vaccine in adult and paediatric IBD patients treated with anti-TNF fails to yield adequate immunologic response after primary vaccination (9-12). Adequate anti-Hbs levels are not present in approximately half of these patients, and in the pediatric IBD patients on anti-TNF 14% did also not respond to a booster vaccine(9). Response to the hepatitis B vaccine has not yet been investigated in neonates born to mothers treated with anti-TNF during pregnancy. The aim of this study is therefore to assess response to the HBV vaccine in children born to IBD mothers treated with anti-TNF during pregnancy in terms of anti-Hbs levels after the final dose of the hepatitis B vaccine. These outcome measures will be compared to a control group of IBD mothers treated with other medication than anti-TNF and their children.

Study objective

Primary Objective:
- Antibodies to the hepatitis B surface antigen (anti-HBs) levels 30 days after the last hepatitis B vaccine dose (11 months) in children from IBD mothers treated with anti-TNF compared to children from IBD mothers not treated with anti-TNF.

Secondary Objective:
- (if required) anti-HBs levels after HBV booster vaccine in case of primary non-immunity
- Anti-TNF levels from the cord blood, and if required when the child is 3 months old, 6 months old and 12 months old.
- Maternal anti-TNF levels at delivery

Study design

We propose a single center, cross sectional study. Pregnant women with IBD treated with anti-TNF during pregnancy who visit the preconception outpatient clinic (POC) will be informed about this study and asked to participate. These women will be asked if they intend to vaccinate their child according to the national vaccination programme (Rijksvaccinatie programma). We will obtain informed consent and make arrangements for obtaining cord blood and maternal peripheral blood at delivery. An appointment will be made at the Sophia*s Children Hospital when the child is 3 months old, 6 months old and 1 year old. At month 3 and 6, anti-TNF serum levels will be determined if the cord blood

anti-TNF level exceeds 3 µg/mL and at 12 months anti-Hbs levels will be assessed. The anti-TNF level assessment is part of standard medical care.

Study burden and risks

Study subjects (mother and child) will not have direct benefits from participating in this study. The burden associated with this study entails a visit at the Sophia Children*s Hospital when the child is 12 months old. At this visit, a blood sample will be obtained for assessment of anti-HBs levels. If the child proves to be non-immune for HBV, 4 weeks after a HBV booster vaccination another appointment at the Sophia*s Children Hospital will be made to obtain another blood sample. The cord blood and possible follow up visits to obtain blood to assess the anti-TNF levels are part of standard medical care and thusly do not count as burden for this study.
This study is exclusively bound to this specific population of pregnant IBD patients and their children. Data from other studies with a similar research question in adults and older children cannot be extrapolated to this population, because of their age and underlying disease. The aimed study population in this study are healthy neonates, born with clinically significant immunosuppressive medication.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

's Gravendijkwal 230
Rotterdam 3015 CE
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

's Gravendijkwal 230
Rotterdam 3015 CE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Study group: IBD mother must be treated with anti-TNF (infliximab or adalimumab) during (part of) the pregnancy
- Control group: IBD mother not treated with anti-TNF (any other IBD medication)
- Live birth

Exclusion criteria

- incapacity to understand the informed consent
- Maternal HBV, HCV or HIV infection
- Other immunecompromising conditions in the child
- not intending to vaccinate child according to the Dutch National Vaccination Programme in Dutch: *Nederlandse Rijksvaccinatieprogramma*

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-05-2014

Enrollment:	24
Type:	Actual

Ethics review

Approved WMO Date:	14-04-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
CCMO	NL47460.078.13