PreCARA: Preconception Counselling in Active Rheumatoid Artritis and other chronic inflammatory arthritides; Preconception counselling for women with rheumatoid arthritis (RA) or another chronic inflammatory arthritis and a pregnancy wish, which is evaluated in a prospective observational study monitoring pregnancy, delivery, postpartum period of the mother, and (growth) parameters of the child.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON43796

Source
ToetsingOnline

Brief title
PreCARA

Condition

- Autoimmune disorders
- Pregnancy, labour, delivery and postpartum conditions

Synonym
chronic inflammatory arthritis, Rheumatoid Arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Een éénmalige subsdie van de Nederlandse Vereniging voor Reumatologie (beroepsvereniging) in 2009. Momenteel wordt het onderzoek uit eigen middelen en uit een subsidie van het Reumafonds bekostigd. ,UCB Pharma

Intervention

Keyword: Chronic inflammatory arthritis, Preconception counselling, Pregnancy, Rheumatoid Arthritis, TNF alfa inhibitors

Outcome measures

Primary outcome

The number of pregnancies

Secondary outcome

Pregnancy outcome for mother and child, especially if conceived under anti-TNFα

treatment and immunological, pharmacological and (social and physical) health

issues of the mother and child before, during and after pregnancy.

Study description

Background summary

Several rheumatic diseases involve chronic inflammation of one or more joints.
The most common of these is Rheumatoid Arthritis (RA). Other examples are

juvenile idiopathic arthritis, spondylarthritides, and psoriatic arthritis. In essence these autoimmune diseases are all systematically active and can affect a variety of organs.
Pregnancy is a very particular condition that can spontaneously reduce the activity of RA. This phenomenon had been investigated in the PARA-study (Pregnancy-induced Amelioration of Rheumatoid Arthritis study). This nationwide prospective cohort study has resulted in some new findings until now. A specific observation was that one out of five patients (20%) was visited preconceptionally but stopped attempts to become pregnant because of severe disease activity after altering medication. These women had to postpone or gave up their pregnancy wish, due to limited treatment options at the time compatible with pregnancy. Also a lower fecundity as shown in previous studies accounts for smaller families of RA patients. Time to pregnancy (TTP) is longer in RA patients, compared to the general population. This prolonged TTP in RA is, among others, related to higher disease activity, and preconceptional use of NSAID*s and prednisone (>7.5 mg daily). Reductions in fertility rate have been shown in other chronic inflammatory arthritides as well.
In the last decade new treatment options for chronic inflammatory arthritides, the so-called biologicals, have become available. During pregnancy the most experience has been gained with anti-TNF alpha (anti tumour necrosis factor alfa) therapy. In the USA, it has been approved for use during pregnancy as a FDA (Food and Drug Administration) class B (e.g. Animal studies have revealed no evidence of harm to the fetus, however, there are no adequate and well-controlled studies in pregnant women, or, animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the foetus in any trimester). Registry studies show that anti-TNFα use seems to be safe during pregnancy in humans also. Furthermore, anti-TNF alfa therapy has been used intentionally preconceptionally to improve the chance of pregnancies in women with recurrent spontaneous abortions. However, some case-reports have been published with adverse pregnancy outcomes, although it is presumed that these adverse outcomes are no different than in other RA patients. Since no randomized controlled trials can be done during pregnancy, circumstantial evidence has led to decision making in daily practice. In case of high disease activity use of anti-TNFα to control disease activity outweighs the risk of potential harm of the foetus. It should nevertheless be taken into account that placental transfer of biologicals from mother to fetus starts at the beginning of the second trimester and increases until term when maternal and fetal serum levels are equal or even higher in cord serum. For this reason use of biologicals is discouraged after the first trimester. In some cases a biological is continued up till week 30 of gestation because the most markedly increase in placental transfer takes place after this period. The biological Certolizumab forms an exception, as it was recently found that this hardly crosses the placental barrier at all
In the ErasmusMC a protocol was developed to standardize care for patients with RA or another chronic inflammatory arthritis. This protocol will be evaluated in the PreCARA study. This study is a continuation of the previous PARA study,

but focuses on a broader group of patients, namely all patients with chronic inflammatory arthritis who want to become pregnant. We aim to provide national guidelines for rheumatologists dealing with patients with these conditions, based on the findings of PreCARA study.

Study objective

In the present study we will evaluate the standardized care protocol developed in our outpatient clinic, intended to guide counselling for medication use prior to pregnancy. This protocol guides treatment decisions based on disease activity, including prescription of anti-TNF therapy. Disease activity, fertility, pregnancy outcome and development of the children will be monitored frequently.

Primary objective:
To evaluate the number of pregnancies in women with RA or another chronic inflammatory arthritis and a pregnancy wish, by evaluating a recently implemented protocol in the department of rheumatology at the ErasmusMC intended for adequate preconceptional counselling by rheumatologists and gynaecologists.
This will eventually lead to the development of national guidelines for preconceptional advice in women with chronic inflammatory arthritis and a pregnancy wish.

Secondary objective:
To prospectively observe pregnancy outcome from mother and child, especially if conceived under anti-TNFα treatment and prospectively observe immunological, pharmacological and (social and physical) health issues of the mother and child before, during and after pregnancy.

Study design

Study design: Prospective observational study.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: The treatment decision is made by the consulting rheumatologist and will be guided by standard health care considerations. Women are free to consent or refuse the offered treatment proposal. Because of the scarce data on use of biologicals in the (pre)conception period, they are asked to give their informed consent in case of use of anti-TNFα treatment.

The burden of regular care:
For rheumatic diseases
1. Consultation, and physical examination at inclusion and subsequently at

every visit (each 3 months) by rheumatologist.
2. Consultation gynaecologist, and 'zwangerwijzer' spreekuur
3. Consultation obstetrician
4. Consultation clinical geneticist (if necessary)
5. Blood samples each 3 months for monitoring disease activity and treatment toleration

The extra burden resulting from the participation in this study will include:
1. Filling out questionnaires at inclusion and subsequently at every visit (each 3 months) at rheumatology department
2. Extra blood samples each 3 months (besides regular blood draw, same needle prick)
3. Complete growth-curves of the child (by parents)

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

4.2 Inclusion criteria, mother:
1) Chronic inflammatory arthritis,
2) > 18 years of age,
3) a wish to conceive,
4) good understanding of the Dutch language, in writing and speech.;N.B. 150 patients with Rheumatoid Arthritis (RA) will be included. Inclusion of patients with other arthritides will close once 150 RA patients have been included.

Exclusion criteria

none

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-08-2011
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO

Date:	25-05-2011

Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-12-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-09-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-01-2017
Application type:	Amendment
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
ClinicalTrials.gov	NCT01345071
CCMO	NL32225.078.10