T4Life trial.

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In euthyroid women with thyroid autoimmunity and recurrent miscarriage, levothyroxine started preconceptional, increases live births beyond 24 completed weeks by at least 20%, compared to placebo.

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON20417

Bron
Nationaal Trial Register

Verkorte titel
T4Life trial

Aandoening

Recurrent miscarriage Thyroid auto-immunity Live birth rate Levothyroxine

Ondersteuning

Primaire sponsor: Academic Medical Centre
Overige ondersteuning: Fonds NutsOhra
Jan Dekker en dr. Ludgardine Bouwmanstichting

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Live birth beyond 24 weeks.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale:

The presence of thyroid antibodies in euthyroid women is strongly associated with recurrent miscarriage (RM) and pregnancy complications like preterm birth and postpartum thyroiditis. Until now no randomized controlled trial exists for endocrine treatment of women with recurrent miscarriage and thyroid autoimmunity. Thyroid peroxidase antibodies (TPO-Ab) are present in 4-14% of fertile women. In clinical practice, thyroid antibodies can be found in women with RM. High prevalences have been described varying from 20 till 36%. But although thyroid hormone supplementation is sometimes prescribed in this subgroup, it is still unclear whether treatment will actually improve pregnancy outcomes. Therefore, we have designed a randomized double blind placebo controlled clinical trial to assess the efficacy of thyroid hormone supplementation, as compared with placebo, on the live birth rate in women with at least 2 preceding miscarriages and the effect on adverse pregnancy complications.

Objective:

To assess improvement in live birth rate and pregnancy outcome after levothyroxine supplementation.

Study design:

Randomised double blind placebo controlled multi centre clinical trial.

Study population:

Women with recurrent miscarriage, i.e. at least 2 miscarriages, aged 18-42 years. Women will be recruited in the Netherlands (Coordinating Centre Academic Medical Centre, Amsterdam) and internationally.

Intervention:

The intervention group receives levothyroxine, and the control group receives placebo of

identical appearance.

Main study parameters/endpoints:

Primary outcome measure: live birth rate.
Secondary outcome measures: miscarriage rate, preterm birth, any maternal or neonatal adverse pregnancy outcomes.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

Women with RM receive standard diagnostic care. The risks and burden of participating in the trial are small. After a complete diagnostic work-up for recurrent miscarriage, the women will be randomized for preconceptual use of levothyroxine versus placebo. The outcome of that particular next pregnancy will be followed. The (minimal) risk of participation is the risk of thyroid hormone use. Substantial evidence exists that thyroid hormone supplementation is safe to the mother and foetus as a treatment for hypothyroidism. For the indication thyroid autoimmunity, clinicians sometimes already prescribe levothyroxine; no adverse effects are known or reported in the literature. And no adverse effects have been described in studies of women with thyroid autoimmunity being treated with levothyroxine.
Women are euthyroid and are given a small dose of levothyroxine; we expect the thyroid hormone levels to stay in the reference interval.

Doel van het onderzoek

In euthyroid women with thyroid autoimmunity and recurrent miscarriage, levothyroxine started preconceptional, increases live births beyond 24 completed weeks by at least 20%, compared to placebo.

Onderzoeksopzet

1. 12 weeks of pregnancy;

2. 24 weeks of pregnancy;

3. End of pregnancy.

Onderzoeksproduct en/of interventie

Levothyroxine tablets started preconceptually after diagnostic work up for recurrent miscarriage till the end of the next pregnancy.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Women with RM and thyroid autoimmunity. Recurrent miscarriage is defined as two or more miscarriages. TPOAb positivity is defined as euthyroid with presence of TPO antibodies. This will be defined according to the cut off levels of the coordinating or cooperating centres. Most commonly used are cut off levels from 60 kU/l or 100kU/l;

2. Age 18 - 42 years at randomisation;

3. Willing and able to give informed consent (IC).

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Antiphospholipid syndrome (lupus anticoagulant and/ or anticardiolipin antibodies IgG or IgM);

2. Other auto-immune conditions, diabetes mellitus, diabetes gravidarum, thyroid disease different then isolated thyroid autoimmunity;

3. Abnormal TSH. This is defined as a TSH level different then the centre specific cut- off levels;

4. Previous enrolment in the T4LIFE-trial;

5. Contraindications to levothyroxine use: Adrenal or pituitary disorders, untreated Acute cardiac arrest;

6. Acute pancreatitis;

7. Acute myocarditis.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-02-2013
Aantal proefpersonen:	240
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:	21-03-2012
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3213
NTR-old	NTR3364
Ander register	EudraCT : 2011-001820-39
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A