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.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20417

Source
Nationaal Trial Register

Brief title
T4Life trial

Health condition

Recurrent miscarriage Thyroid auto-immunity Live birth rate Levothyroxine

Sponsors and support

Primary sponsor: Academic Medical Centre
Source(s) of monetary or material Support: Fonds NutsOhra
Jan Dekker en dr. Ludgardine Bouwmanstichting

Intervention

Outcome measures

Primary outcome

Live birth beyond 24 weeks.

Secondary outcome

1. Miscarriage rate; 2. Any adverse pregnancy complications (preterm birth, preeclampsia, gestational diabetes, intrauterine growth retardation, pregnancy induced hypertension, birth weight, placental abruption, placenta praevia, perinatal mortality, mode of delivery, respiratory distress, low Apgar scores, admission NICU, breech position, neonatal thyroid dysfunction and malformations, postpartum thyroid disease); 3. Time to pregnancy (defined as the interval between thyroid function test and the month of conception of the next pregnancy).

Study description

Background summary

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.

Study objective

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.

Study design

1. 12 weeks of pregnancy;

2. 24 weeks of pregnancy;

3. End of pregnancy.

Intervention

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

Contacts

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Eligibility criteria

Inclusion criteria

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).

Exclusion criteria

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.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-02-2013
Enrollment:	240
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	21-03-2012
Application type:	First submission

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
NTR-new	NL3213
NTR-old	NTR3364
Other	EudraCT : 2011-001820-39
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A