**O-021 Levothyroxine in Euthyroid Thyroid Peroxidase Antibody positive Women with Recurrent Pregnancy Loss: a multicentre, randomised, double-blind trial (T4LIFE trial)**

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**Study question:** Does levothyroxine treatment increase live birth rates in thyroid peroxidase antibodies (TPO-Ab) positive women with recurrent pregnancy loss (RPL) and normal thyroid function?

**Summary answer:** Levothyroxine treatment did not result in higher live birth rates in women with RPL positive for TPO-Ab and a normal thyroid function, compared to placebo.

**What is known already:** Women positive for TPO-Ab have a higher risk of RPL. Levothyroxine supplementation has been proposed to reduce the risk of pregnancy complications. Evidence is limited whether levothyroxine treatment improves pregnancy outcomes in TPO-Ab positive women with RPL.

**Study design, size, duration:** We conducted an international double-blind trial. Between January 2013 and September 2019, we randomly assigned 187 women to receive levothyroxine (94 women) or placebo (93 women). Before conception, women were randomly assigned in a 1:1 ratio to levothyroxine or placebo orally once daily. The daily dose of levothyroxine was based on preconception TSH level and ranged from 0.5 to 1.0 μg/kg body weight. Levothyroxine or placebo was continued until the end of pregnancy.

**Participants/materials, setting, methods:** Patients with two or more pregnancy losses underwent diagnostic testing for RPL. Women with a normal TSH level and positive for TPO-Ab were eligible for the study. Antiphospholipid syndrome was an exclusion criterion. The primary outcome was live birth, defined as the birth of a living child beyond 24 weeks of gestation. Secondary outcomes included ongoing pregnancy, pregnancy loss, preterm delivery, adverse events and time to conception leading to live birth.

**Main results and the role of chance:** Live birth occurred in 47 women (50%) in the levothyroxine group and in 45 women (48%) in the placebo group (risk ratio, 1.03; 95% confidence interval [CI], 0.77 to 1.38; absolute risk difference 1.6%; 95% CI, 1.2.7% to 15.9%). There were no significant differences in any secondary outcomes. In both groups seven adverse events were reported, none of them directly related to the study procedure.

**Limitations, reasons for caution:** The slow recruitment forced us to stop the trial prematurely. With this sample size we are not able to fully account for dropouts and the estimates have wide 95% confidence intervals. Detection of a difference of 5% in live birth rate would have required inclusion of more than 3000 women.

**Wider implications of the findings:** Routine use of levothyroxine in women with RPL and normal thyroid function positive for TPO-Ab is not recommended. Our results are in line with previous trials in TPO-Ab positive women with a history of infertility or pregnancy loss or undergoing in vitro fertilization.

**Trial registration number:** Netherlands Trial Register (NTR3364).