Stop or Go? Relapse prevention training with guided tapering of antidepressants during pregnancy. A pragmatic multicenter RCT to investigate risk and benefits for mother and child.

Gepubliceerd: 16-07-2014 Laatst bijgewerkt: 18-08-2022

1) Tapering of SSRIs with added preventive cognitive therapy (CT) increases the risk of clinically relevant maternal relapse of depression in excess of [absolute] 15% compared to continuation of SSRIs. If rejected, then discontinuation is deemed non…

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

Samenvatting

ID

NL-OMON23074

Bron
NTR

Verkorte titel
Stop or go?

Aandoening

Pregnant women, depressive symptoms, anxiety, antidepressants, SSRI, tapering of medication

Ondersteuning

Primaire sponsor: ErasmusMC
Overige ondersteuning: ZonMW

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Risk (cumulative incidence) of relapse of maternal depressive disorder (as defined by the Structured Clinical Interview for DSM disorders) during pregnancy and up to 3 months postnatal.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale:

About 2% women in the Netherlands use Selective Serotonin Reuptake Inhibitors (SSRIs) during their pregnancy for symptoms of depression and/or anxiety. SSRI use in pregnancy is controversial. On the one hand SSRIs may be toxic to the intrauterine developing child, while on the other hand, relapse of depression and/or anxiety during pregnancy holds risks for both mother and child. Among patients and professionals there is an urgent need for evidence from randomized studies to make rational decisions regarding continuation or tapering of SSRIs during pregnancy. No such studies exist to date.

Objective:

The aim of this study is to investigate the effect of preventive cognitive therapy with guided tapering of SSRIs in early pregnancy as compared to continuation of SSRIs during pregnancy. We will study effects on both mother and child with a pragmatic approach.

Our hypotheses are:

1) Tapering of SSRIs with added preventive cognitive therapy (CT) increases the risk of clinically relevant maternal relapse of depression in excess of [absolute] 15% compared to continuation of SSRIs. If rejected, then discontinuation is deemed non-inferior with regard to relapse risk;

2) Tapering of SSRIs is better than continuation of SSRIs with respect to child development;

3) Assuming no relevant effects of discontinuation on the mother and no effects on the child, discontinuation decreases total costs per woman and child on a 3 months and projected long

term base.

In absence of clinical differences between the two options, tapering of SSRIs will be declared preferential during pregnancy.

Study design:

A nationwide pragmatic multi-center randomized controlled non-inferiority trial (RCT).

Study population:

The study population consists of 200 women who are between 8-16 weeks pregnant and use SSRIs without clinically relevant depressive symptoms.

Intervention:

After informed consent, women will be randomly allocated into two groups:

1. Preventive cognitive therapy with gradual, guided discontinuation of SSRI under clinical management (intervention group);

2. Continuation of SSRI (control group).

Main study parameters/endpoints:

Primary outcome:

Risk (cumulative incidence) of relapse of maternal depressive disorder (as defined by the Structured Clinical Interview for DSM disorders) during pregnancy and up to 3 months postnatal.

Secondary outcomes:

1. Child condition at birth (Apgar, gestational age, birth weight, head circumference);

2. Child neurodevelopmental outcome at 3 months (General Movements);

3. Child behaviour (CBCL) at 18 months;

4. Cost effectiveness (including indicated second echelon care, hospital delivery and clinical child observation in case of SSRI use).

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

All participants in the study receive regular check up on the potential return of their depressive symptoms. The main risk in this study involves the tapering of medication in women who are mentally stable. Although tapering of antidepressant medication in mentally stable patients is part of evidence based clinical practice, it could introduce relapse of previous depressive symptoms. We realize that in pregnant women this involves risks for the mother and her unborn child. Therefore, each patient will be critically evaluated by an experienced psychiatrist/clinical psychologist at inclusion, to judge whether it is clinically justified to taper antidepressant medication. If so, antidepressants will be tapered with close monitoring by a general practitioner or psychiatrist, and additional preventive CT will be provided. The provision of preventive CT in addition to tapering medication is in accordance with (inter)national guidelines (Multidisciplinary Dutch guidelines 2013, APA 2010, NICE 2009)1,2,3.
Of note is that in both randomized groups concomitant therapy is allowed in this pragmatic trial, e.g. the administration of benzodiazepines.
Additional burdens without risks will be:

1. Blood sampling of the woman at inclusion;

2. A structured psychiatric interview of the woman at inclusion (30-90 minutes) and at 12 weeks after delivery (+/- 30 minutes);

3. Questionnaires at fixed time points: inclusion, 24 and 36 weeks pregnancy, 4 and 12 weeks and 18 months after delivery (+/- 30 minutes);

4. Collection of meconium of the newborn by the parents;

5. Collection of breast milk when breastfeeding;

6. Collection of placenta and cord blood (if possible);

7. Collection of hair (+/- 1 cm2) and a buccal swab at 3 months after delivery of both mother and child;

8. The child born from the included woman will be videotaped in a non-invasive home observation at 3 months of age (30-60 minutes) to measure general movements of the child. The mother is allowed to be present during the assessment.

A potential benefit of participating in this study might be the superiority of the intervention (i.e. tapering of SSRI with additional preventive CT) compared to treatment as usual with respect to maternal and child health outcome. The study guarantees access to preventive CT therapists without additional costs and waiting lists for participants who are allocated to the intervention arm.

Doel van het onderzoek

1) Tapering of SSRIs with added preventive cognitive therapy (CT) increases the risk of clinically relevant maternal relapse of depression in excess of [absolute] 15% compared to continuation of SSRIs. If rejected, then discontinuation is deemed non-inferior with regard to relapse risk.

2) Tapering of SSRIs is better than continuation of SSRIs with respect to child development.

3) Assuming no relevant effects of discontinuation on the mother and no effects on the child, discontinuation decreases total costs per woman and child on a 3 months and projected long term base.

In absence of clinical differences between the two options, tapering of SSRIs will be declared preferential during pregnancy.

Onderzoeksopzet

T0: Inclusion: SCID, HAM-D, Mind2Care, STAI, EPDS, PSS, TIC-P, EQ-5D-5L, bloodsample;

T1: 24 weeks: CTQ, EPDS, STAI 6-item, PSS, EQ-5D-5L;

T2: 36 weeks: HAM-D, EPDS, PSS, STAI 6-item, TIC-P, EQ-5D-5L;

T3: Delivery: registered details;

T4: 4 weeks after delivery: EPDS, PSS, STAI 6-item, TIC-P, EQ-5D-5L;

T5: 12 weeks after delivery: SCID, HAM-D, EPDS, PSS, STAI 6-item, TIC-P, EQ-5D-5L, GM, hair cortisol;

T6: 18 months after delivery: CBCL, C-TRF, LDS;

T7: 24 months after delivery: information of the CJG.

Onderzoeksproduct en/of interventie

After informed consent, women will be randomly allocated into two groups:

1) Preventive cognitive therapy with gradual, guided discontinuation of SSRI under clinical

management (intervention group);

2) Continuation of SSRI (control group).

Contactpersonen

Publiek

Antwoordnummer 55, 3000 WB, Rotterdam
N. Molenaar
Erasmus MC, afdeling Psychiatrie
Westzeedijk 118/Wk-207
Rotterdam 3000 WB
The Netherlands
0649844950

Wetenschappelijk

Antwoordnummer 55, 3000 WB, Rotterdam
N. Molenaar
Erasmus MC, afdeling Psychiatrie
Westzeedijk 118/Wk-207
Rotterdam 3000 WB
The Netherlands
0649844950

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Less than 16 weeks pregnant;

2. SSRI use for depressive disorder.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Insufficient proficiency in Dutch or English;

2. Multiple pregnancies (because of increased risk for adverse birth outcomes that might confound statistical analyses);

3. Severe medical conditions that involve treatment decisions overriding research participation;

4. Current relapse of depression after previous attempts to taper SSRIs;

5. Current other psychiatric disorders (i.e. psychosis, bipolar disorder, severe obsessive-compulsive disorder, substance abuse, suicidality and/or serious self-harm).

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Enkelblind
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-01-2015
Aantal proefpersonen:	200
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	16-07-2014
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	NL4551
NTR-old	NTR4694
Ander register	2014-003086-25 : EudraCT

Resultaten