A randomized, double-blind, placebo-controlled, pilot trial of probiotics in pregnant women with symptoms of anxiety and depression.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON43160

Source
ToetsingOnline

Brief title
PIP (Probiotics In Pregnancy)

Condition

- Other condition
- Pregnancy, labour, delivery and postpartum conditions
- Mood disorders and disturbances NEC

Synonym
anxiety, Depression

Health condition

angstklachten

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universiteit Nijmegen
Source(s) of monetary or material Support: Subsidies zijn aangevraagd;nog niet toegezegd. CMO/METC toestemming is vooraf vereist bij de potentiële subsidiegevers alvorens toekenning van de subsidies

Intervention

Keyword: Anxiety, Depression, Pregnancy, Probiotics

Outcome measures

Primary outcome

The primary outcome is the number of successfully met feasibility criteria

linked to the intervention and the study design.

For a full RCT two groups of 75 women (N = 150 total) need to be included to

reach a significant difference between two groups (placebo vs. probiotics)

regarding reduction of depression symptoms (a priori analysis; with 0:05

significance level, power of 80%, effect size f = 0.187, 25% drop out). The aim

of the present pilot study is to investigate the feasibility of a complete

study. Therefore, ~ 27% of a full study, 20 women per arm (N = 40 total) will

be included.

Secondary outcome

Secondary outcomes are questionnaire data and (microbial) sample data collected

during the perinatal period assessing physical and mental health in mothers and

their children. Questionnaire data pre and post intervention are collected with

the Edinburgh Depression Scale (EDS), Leiden Index of Depression Sensitivity,

Revised (LEIDS-R), Pregnancy Related Anxiety Questionnaire-Revised (PRAQ-R), State-trait Anxiety Inventory (STAI-S), Pregnancy-related daily hassles (PES), Algemene Problemen Lijst (APL), Maternal Antenatal Attachment Scale (MAAS) and Maternal Postnatal Attachment Scale (MPAS). Sleep is measured with the Pittsburgh Sleep Quality Index (PSQI). Biological parameters include maternal hair cortisol, maternal vaginal and intestinal microbial composition, and infant intestinal microbial composition.

Study description

Background summary

Maternal prenatal depression or anxiety during late pregnancy are risk factors for adverse health and behaviour outcomes in offspring. With prevalence rates of prenatal depression or anxiety ranging between 10-20%, attempts to identify feasible and effective interventions to reduce symptoms are priority in the prenatal care and clinical setting. There are indications that probiotics can reduce levels of depression or anxiety. Probiotics ingested by the mother may offer a promising, relatively cheap and accessible intervention to complement current existing effective treatments to reduce symptoms of anxiety or depression during pregnancy. Therefore, this pilot study evaluates the feasibility of a multispecies probiotic intervention in pregnant women, as an adjuvant therapy, to reduce prenatal depression and anxiety, ultimately to improve maternal and infant health.

Study objective

The primary objective is to assess feasibility of a food supplement (multispecies probiotic) placebo-controlled, randomised controlled, double blind intervention in pregnant women in their late second/third trimester of pregnancy, to reduce symptoms of depression and anxiety, in preparation for a larger randomized controlled trial (RCT). Additionally, the potential effectiveness of probiotics will also be recorded.

Study design

Feasibility assessment of a double-blind, placebo-controlled, randomised controlled pilot trial in the prenatal care setting in the Netherlands. One

group (intervention group) orally consume food supplement (multispecies probiotic mixture) and effectiveness will be compared with one group orally consuming placebo (placebo group). A concealed computer generated list is used to randomise participants, with an allocation of 1:1 to the intervention and placebo.

Intervention

Women orally consume multispecies probiotic mixture (2,5 x 109 CFU/g) once-daily versus placebo from 26 weeks gestation until delivery (8-14 weeks). This ensures at least 8 weeks of probiotic intake in case of preterm labour.

Study burden and risks

There is ample evidence that symptoms of anxiety and depression during late pregnancy are risk factors for adverse child health outcomes. The probiotic supplement used in this study is available for consumers on the international market and all bacterial strains have a QPS-status. The latter indicates that the experts of the European Food Safety Authority (EFSA) deems them safe for consumption. Most importantly for this study, to date, probiotic intake has not been associated with severe adverse health effects in the mother, fetus, infant or child and intake of probiotics by healthy (pregnant) subjects is therefore considered safe (Dugoua et al, 2009a ;. Huurre, Laitinen, Rautava , Korkeamäki & Isolauri, 2008; R Luoto, Kalliomäki, Laitinen, & Isolauri, 2010; Snydman, 2008; VandeVusse, Safdar & Hanson, 2013, Rutten et al., 2015).

1) Intervention group:
Disadvantage: Participants will undertake an extra visit to their echo center (Fara, Ede) or to the DPBLab (Radboud, Nijmegen). They will consume a probiotic drink once a day for 8-14 weeks (depending on the time of birth). Participants collect stool samples at home four times (two maternal and two baby stool collections) and complete questionnaires. Further, two vaginal microbiota samples and one hair sample is collected. The disadvantage here is the time invested in the study and routine intake of probiotics. Previous studies with probiotics in pregnant women did not cause serious side effects, women may possibly suffer from bloating, cramps and/or altered bowel habits. The women in the intervention group continue with their standard medical or psychological treatment, and therefore we expect no additional psychological risks.
Advantage: possible reduction in feelings of anxiety and depression, possible improvement of intestinal and vaginal microbiota.
2) Placebo group:
Participants will undertake an extra visit to their echo center (Fara, Ede) or to the DPBLab (Radboud, Nijmegen). They will consume a probiotic drink once a day for 8-14 weeks (depending on the time of birth). Participants collect stool samples at home four times (two maternal and two baby stool collections) and complete questionnaires. Further, two vaginal microbiota samples and one hair

sample is collected. The disadvantage here is the time invested in the study and routine intake of probiotics. The time invested in the study is similar to the intervention group. The women in the control group continue with their standard medical or psychological treatment, and therefore we expect no additional risk in the control group.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Healthy pregnant women in obstetric care in the Netherlands with at least elevated symptoms of depression and/or anxiety (resp. EDS * 10; STAI-S > 40)
2. Women who can start daily probiotic intake from *26 weeks gestational age until delivery (Note: the upper limit of *26 weeks allows time to complete at least 8 weeks of probiotic intake prior to delivery) (Gestation is based on last menstrual period and early ultrasound).

Exclusion criteria

1) Multiple pregnancy (increased obstetric risk);
2) High suicidal risk according to suicidality subscale score on the MINI International Neuropsychiatric Interview;
3) Illegal drug use;
4) Having a psychiatric history on psychoses and bipolar disorder;
5) Medically diagnosed with inflammatory bowel disease;
6) History of major gastro-intestinal surgery (e.g. colectomy);
7) Hypersensitivity or allergy to any ingredients in the probiotic product;
8) History of using oral multi-species probiotic EcologicBarrier;
9) Presently using food containing probiotics (Actimel etc.) and not willing to stop these at least 2 weeks prior to the start of the study;
10) No mastery of the Dutch language.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-04-2017
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	08-12-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-08-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 26403
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL57780.091.16
OMON	NL-OMON26403