The relationship between age at menopause loci and the response of controlled ovarian hyperstimulation in women undergoing IVF: a candidate gene study.

Gepubliceerd: 06-01-2021 Laatst bijgewerkt: 15-05-2024

We hypothesize that presence of genetic variants associated with earlier age of natural menopause might be involved in diminished responsiveness of the ovaries to exogenous FSH stimulation during IVF treatment.

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	-

Samenvatting

ID

NL-OMON28369

Bron
Nationaal Trial Register

Verkorte titel
RiSPONS

Aandoening

Subfertile women who will undergo IVF treatment.

Ondersteuning

Primaire sponsor: Ferring
Overige ondersteuning: Ferring

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The primary outcome parameter is the responsiveness of the ovaries to exogenous FSH stimulation during IVF treatment, i.e. number of retrieved oocytes.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: Over the last decade genome-wide association studies (GWAS) have identified hundreds of common genetic variants (Single Nucleotide Polymorphisms, SNPs) associated with age of natural menopause (ANM). The peri-menopausal stage is preceded by a decrease in fertility eventually leading to sterility in the 10 years before menopause. Poor response to controlled ovarian hyperstimulation (COH) during IVF treatment is a reasonable predictor of diminished ovarian reserve. Therefore, we hypothesize that presence of genetic variants associated with earlier age of natural menopause might also be involved in diminished responsiveness of the ovaries to exogenous FSH stimulation during IVF treatment. In other words, patients that carry more SNPs associated with early age of menopause might as well have a poor response to COH treatment. Consequently, if that is the case, these SNPs might be used as a predictor for ovarian response during IVF treatment using polygenic risk scores.

Objective: In this project, we hypothesize that presence of genetic variants associated with earlier age of natural menopause might be involved in diminished responsiveness of the ovaries to exogenous FSH stimulation during IVF treatment. Furthermore, we aim to investigate whether polygenic risk scores of genetic variants associated with age at natural menopause based on the large-scale GWAS are predictive of the response to IVF stimulation in patients starting their first IVF treatment cycle leading to a more patient-tailored care-setting.

Study design: This candidate gene study will be conducted in a retrospective as well as prospective cohort study.

Study population: Patients will be recruited at the IVF outpatient clinic of the Division of Reproductive Medicine at the Erasmus MC, University Medical Center, Rotterdam. All women with a regular menstrual cycle undergoing their first cycle of IVF because of male infertility or unexplained infertility will be asked to participate in this study.

Study protocol: Baseline characteristics, including medical history, age, BMI, smoking, SES, and endocrine parameters such as FSH, LH, progesterone, estradiol, AMH will be determined. Extra blood samples will be taken during standard blood sampling. DNA will be extracted from peripheral blood, and genotyping shall be executed using Illumina arrays. Standard quality-control procedures are performed. SNPs were selected to be included in the Polygenic

Risk Score calculation based on their p-values in the original GWAS. Patients will undergo hormonal stimulation according to a standard protocol in our clinic. Response to the IVF stimulation in terms of dose of exogenous FSH, number of follicles and number and quality of obtained oocytes as well as pregnancy will be monitored.

Main study parameters: The primary outcome parameter is the responsiveness of the ovaries to exogenous FSH stimulation during IVF treatment, i.e. number of retrieved oocytes. Secondary study parameters are other outcomes of the IVF treatment, described by the number of follicles after stimulation, quality of retrieved oocytes, quality of embryo's as well as pregnancy rate and live-birth rate.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Single blood sampling is needed to execute this candidate gene study, although this will be combined with standard blood sampling women will need to visit the hospital one extra time.

Doel van het onderzoek

We hypothesize that presence of genetic variants associated with earlier age of natural menopause might be involved in diminished responsiveness of the ovaries to exogenous FSH stimulation during IVF treatment.

Onderzoeksopzet

Before IVF treatment the extra blood samples will be taken.

Onderzoeksproduct en/of interventie

Extra blood samples will be taken during standard blood sampling.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- A regular menstrual cycle
- Undergoing IVF because of male infertility or unexplained infertility
- First cycle IVF treatment
- Age between 18 and 45 years at the time of the IVF treatment

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- A history of ovarian surgery, chemotherapy of radiation therapy
- Non Northern European ethnicity

Onderzoeksopzet

Opzet

Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-01-2021
Aantal proefpersonen:	500
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Ethische beoordeling

Positief advies

Datum:	06-01-2021
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 54409
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9173
CCMO	NL75062.078.20
OMON	NL-OMON54409

Resultaten