BRCA mutations and Ovarian ageing in women applying for in vitro fertilization and preimplantation genetiC diAgnosis

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To demonstrate the presence of a reduced age specific ovarian reserve status in BRCA mutation carriers by:1. using serum AMH as ovarian reserve status test. 2. using the antral follicle count (AFC) as ovarian reserve test3. using ovarian response to...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Menopause related conditions
Study type	Observational invasive

Summary

ID

NL-OMON47054

Source
ToetsingOnline

Brief title
BROCA-2 sudy

Condition

- Menopause related conditions

Synonym
ovarian ageing, ovarian reserve

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: BRCA mutation, Ovarian ageing, Ovarian reserve test, Ovarian response

Outcome measures

Primary outcome

Ovarian ageing measured by serum AMH levels.

Secondary outcome

Antral follicle count

Ovarian response (oocytes yielded, MII ooocytes, poor response)

Clinical pregnancy rate

Ongoing pregnancy rate

Study description

Background summary

Timing of menopause is associated with preceding infertility and multiple women's health risks, such as breast, endometrial and ovarian cancer, osteoporosis, cardiovascular diseases, cognition, sexual health and general well being. Therefore, studies on factors that determine age at menopause or ovarian ageing can help us unravel the underlying biological pathways and mechanisms of the associated infertility and health risks.
In recent literature, there remains uncertainty about the impact of BRCA gene mutations on ovarian reserve and age of natural menopause.

In the current study, by assessing the ovarian reserve by using three different parameters (AMH, AFC and ovarian response) we will be able to study the effect of BRCA mutations on ovarian ageing,

The primary hypothesis is that normo-ovulatory women with a deleterious BRCA mutation have lower levels of AMH compared to normal controls, with at least a difference of 0.90 ng/ml, suggesting an effect size of approximately five years in menopausal age.

Study objective

To demonstrate the presence of a reduced age specific ovarian reserve status in BRCA mutation carriers by:
1. using serum AMH as ovarian reserve status test.
2. using the antral follicle count (AFC) as ovarian reserve test
3. using ovarian response to ovarian hyperstimulation for IVF as proxy variable of ovarian reserve status.

Study design

International, multicenter and observational study with an invasive measurement (serum sampling)

Study burden and risks

The risks associated with participation are negligible.

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

Case group:
Female age * 40 years
Regular menstrual cycles (i.e. mean cycle length of 21-35 days)
First IVF with ICSI and PGD treatment cycle due to a female pathogenic BRCA mutation
Written informed consent;Control group:
Female age * 18 years and * 40 years
Regular menstrual cycles (i.e. mean cycle length of 21-35 days, with the next menstrual period predictable within a 7 days* time frame)
First IVF with ICSI and PGD treatment cycle due to an indication unsuspected for reduced ovarian reserve status
Written informed consent

Exclusion criteria

Case group:
Ovarian surgery
Chemotherapy
Radiation therapy to the pelvis, lower abdomen or total body radiation
Known female endocrine or autoimmune abnormalities (i.e. Cushing syndrome, type I Diabetes Mellitus, hypothyroidism, hyperprolactinemia, adrenal insufficiency, hypoparathyriodism, myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus)
Body Mass Index > 30 kg/m2
Polycystic Ovarian Syndrome (Rotterdam criteria)
Early follicular FSH > 15 IU/L
Known HIV infection
Known genetic abnormalities, suspected for subfertility (structural or numerical abnormalities of the X-chromosome (i.e. Turner*s syndrome, fragile X syndrome), or abnormalities of human autosomal functionally relevant genes suspected for subfertility, other than a BRCA mutation. ;Control group:
Ovarian surgery
Chemotherapy
Radiation therapy to the pelvis, lower abdomen or total body radiation
Known female endocrine or autoimmune abnormalities (i.e. Cushing syndrome, type I Diabetes Mellitus, hypothyroidism, hyperprolactinemia, adrenal insufficiency, hypoparathyriodism, myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus)
Body Mass Index > 30 kg/m2
Polycystic Ovarian Syndrome (Rotterdam criteria)
Early follicular FSH > 15 IU/L
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of the X-chromosome (i.e. Turner*s syndrome, fragile X syndrome), or abnormalities on human autosomal functionally relevant genes suspected for subfertility.
PGD requested for structural chromosomal abnormalities

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	29-10-2014
Enrollment:	109
Type:	Actual

Ethics review

Approved WMO Date:	10-07-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-06-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	22-08-2018
Application type:	Amendment

Review commission: METC Universitair Medisch Centrum Utrecht (Utrecht)

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
CCMO	NL45629.041.14