peri-IMplantation Profile of Endometrial Transcription

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Endocrine disorders of gonadal function
Study type	Observational invasive

Summary

ID

NL-OMON38230

Source
ToetsingOnline

Brief title
IMPECT

Condition

- Endocrine disorders of gonadal function
- Uterine, pelvic and broad ligament disorders

Synonym
recurrent implantation failure

Research involving
Human

Sponsors and support

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

Intervention

Keyword: endometrium, gene expression, implantation failure

Outcome measures

Primary outcome

Validation of our initial findings of a molecular signature which can be distinguish between normally receptive and less-receptive endometrium (06/101/K)

Secondary outcome

- To identify differences between normally receptive and less-receptive endometrium by protein expression.

- To implement our findings of the molecular signature in the IVF patient population. Comparing gene expression results betweeen IVF patients that conceived within 3 IVF attempts and patients who didn't (implantation failure).

Study description

Background summary

Implantation failure constitutes the major limiting step in in-vitro fertilization (IVF) success rates and it is a considerable cause of frustration to patients and clinicians. The endometrium becomes receptive in preparation for embryo implantation during a restricted period, which is referred to as a *window* of receptivity and takes place from approximately day 19-24 in a normal menstrual cycle. Up to now, no individual factors have been identified to be crucial for implantation in the human. However, given the complexity of the process of implantation and its crucial role in human survival, it is unlikely that a single marker of great clinical significance will be identified. Microarray analysis enables an approach from a global genomic perspective. Our study (06/101/K) provided a comparison of endometrial gene expression during the window of implantation in women with recurrent

implantation failure (RIF) and controls. The study reports the biggest set of microarray data on endometrial gene expression in women with implantation failure to date. We have shown that the expression profile of several promising genes are predictive of the recurrent implantation failure. Above a certain cut-off the predictive accuracy to correctly determine whether the endometrial sample is taken from a good receptive endometrium or from women with recurrent implantation failure is 94%.

Study objective

In order to confirm and externally validate the novel panel of genes identified in our study (06/101/K) to be significantly predictive of recurrent implantation failure, we will recruit 50 additional subjects treated by IVF who have undergone at least 3 consecutive fresh good quality embryo transfers without achieving pregnancy, 50 controls, defined according to the same criteria as in the development study cohort, i.e.: who were formerly treated by ICSI for severe male factor infertility only and who achieved a healthy live birth after the first or second treatment cycle and 50 references; patients who conceived and gave birth to a healthy child within 3 IVF attempts.
This additional recruitment is necessary to confirm and extent our initial findings of a molecular signature which can be distinguish between good receptive and less-receptive endometrial tissue.

Study design

The study design is a patientcontrol study (comparison of endometrial receptivity markers of patients with RIF vs. controls vs. references).

Women who attended our Clinic for IVF or ICSI treatment with recurrent implantation failure, women who achieved a healthy live birth after ICSI treatment for severe male infertility and women conceived and gave birth to a healthy child within three IVF attempts will be asked to participate in our study. Patients will be asked to give written informed consent for the endometrail biopsie and the storage of samples for research purposes.

Women who attend the study will perform at home ovulation predictor tests in urine from cycleday 10 till a positive test. Six or seven days after a positive test the endometrial biopsy is sheduled. Analysis of endometrial gene expression profiles in the endometrial tissue will be performed by microarray and PCR and protein expression by Western blotting.

Study burden and risks

The study includes an endometrial biopsy. This is a minimal invasive method with minimal risks. The most common (temporary) complain is abdominal pain or discomfort. Rare is dizziness, infection, bleeding or very rare a perforation

of the uterus. No negative effect on pregnancy rate from this intervention in following cycles has been reported.

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100/ Postbus 85500
3508 GA Utrecht
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100/ Postbus 85500
3508 GA Utrecht
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

All groups:
- age from 18 till 38 years at moment of IVF or ICSI treatment
- regular mentrual cycle (25-35 days);Study group:
Women who have not achieved a pregnancy, despite at least three fresh embryo transfers in an IVF or ICSI treatment.
- An abortion will be regarded as a pregnancy.
- A chemical pregnancy will not be regarded as a pregnancy.;Control group
Women who conceived after the first or second ICSI treatment for male factor infertility and

who have delivered a healthy baby.;Reference group
Women who conceived and have delivered a healthy baby within three IVF attempts.

Exclusion criteria

All groups:
- Use of oral anticonceptives or an intra-uterine device
- Difficulty in communicating in Dutch or English
- Poor ovarian response after adequate ovarian stimulation
- Smoking;Study group
- PESA (percutaneous epididymal sperm aspiration) / MESA (microsurgical epididymal sperm aspiration / TESE (testicular sperm extraction)
- Abortion following the IVF or ICSI treatment
- A known cause of recurrent implantation failure detected during pre-inclusion screening.
- Poor embryo quality;Control group
- Other causes of infertility than severe male infertility.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-10-2011
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO Date:	09-06-2011
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	03-05-2012
Application type:	Amendment
Review commission:	METC NedMec

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	NL30743.041.10