Towards a new technique for pre-implantation genetic embryo screening in IVF, pilot phase

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The objective of this study is to evaluate a new and less invasive method of PGS. The new PGS technique will analyse a nucleus of a blastomere that was obtained by nuclear extraction rather than by biopsy of a whole blastomere.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Interventional

Summary

ID

NL-OMON30715

Source
ToetsingOnline

Brief title
Towards a new technique for PGS, pilot

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Abortions and stillbirth
- Sexual function and fertility disorders

Synonym
implantation failure, subfertility

Research involving
(Surplus) Embryos

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Ministerie van OC&W,grant zal worden aangevraagd

Intervention

Keyword: chromosomal abnormalities, embryo, enucleation, pregnancy rates

Outcome measures

Primary outcome

Comparison of successful FISH analyses and the morphology and development of

these embryos with biopsy-PGS and control embryos.

Secondary outcome

Description of a succesful enucleation-PGS procedure

Study description

Background summary

The success rate of in vitro fertilization (IVF) procedures is determined by many variables. One important variable is the selection of a high quality embryo for transfer into the uterus. It is however, difficult to assess embryo quality. Currently the only routinely used parameters are morphologic features assessed by microscopy. A high percentage of human embryos contain aneuploid cells which is likely to affect pregnancy rates. Pre-implantation genetic screening (PGS) can detect such an aneuploidy by using fluorescent in situ hybridization (FISH) on a single cell obtained from an embryo. Hence, PGS allows for screening and selection of IVF embryos based on chromosomal integrity. It is assumed that such a selection of the *best* embryo for transfer would lead to an increase in ongoing pregnancy rate and a decrease in the number of miscarriages. Randomized controlled trials could however not detect an inceased pregnancy outcome in the biopsy PGS group. Hence the benefits of PGS are not yet established. The PGS procedure is thought to be safe since biopsied embryos show normal outgrowth to blastocysts. However, subsequent outgrowth to later developmental stages has not been analysed independently of embryo selection. It is possible that several steps in the biopsy procedure cause small traumas to the embryo that may result in a decreased implantation potential even though its outgrowth to a blastocyst is not affected. Such negative effects may counterbalance the positive effect of PGS selection and hence it seems important to explore less traumatic nuclear

extraction procedures to be used in PGS.

Study objective

The objective of this study is to evaluate a new and less invasive method of PGS. The new PGS technique will analyse a nucleus of a blastomere that was obtained by nuclear extraction rather than by biopsy of a whole blastomere.

Study design

The study will consist of a pilot project to investigate the methodological aspects of the enucleation procedure, and if successful, permission for a subsequent prospective randomized trial (RCT) with IVF patients, using enucleation-PGS will be requested from the CCMO. The pilot study will have to provide answers on how to perform the enucleation and a validation of the FISH procedure as well as whether outgrowth of enucleated embryos to blastocysts is normal.

Intervention

For enucleation in spare-embryos, a sharp micro-pipette is used to isolate the nucleus and the remaining cytoplasm from a single blastomere and in biopsy-PGS a whole blastomere is isolated using standard biopsy techniques. The nuclei are used for FISH analysis with 10 chromosomal probes and the remainder of the embryo is used in a comparative outgrowth test with control embryos.

Study burden and risks

Biopsy-PGS does not result in an increased number of abnormal offspring. Biopsy of a blastomere does not lead to differences in in-vitro development but is suspected to reduce the developmental potential of embryos. We expect the enucleation procedure to be saver and less traumatic compared to a conventional biopsy procedure. This study will use spare embryo's and the donating patients will thus not receive any burden or risks.

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

standard indication IVF/ICSI
written informed consent

Exclusion criteria

Abnormal parental karyotype/genetics if known
oocyte donation
PESA/MESA
two previously failed IVF treatments

Study design

Design

Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-08-2007
Enrollment:	435
Type:	Actual

Ethics review

Approved WMO Date:	12-06-2007
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-12-2007
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	NL11470.000.07