ISRCTN11455145 https://doi.org/10.1186/ISRCTN11455145

Spindle transfer for the treatment of infertility problems associated to poor egg quality: a pilot trial

Submission date
15/02/2018

Recruitment status
No longer recruiting

Registration date
20/02/2018

Overall study status
Ongoing

Last Edited
04/04/2024

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Assisted reproductive treatments can be performed to help achieve pregnancy. Poor egg quality is one of the main causes of repeated failures in assisted reproduction treatments. The quality of the eggs is mainly determined by small organelles named mitochondria (the energy suppliers of the cells), together with other factors present in the cytoplasm of the eggs. Unfortunately, many times, patients who are dealing with poor egg quality experience several IVF failed attempts due to impaired embryo development, and have to be treated with conventional egg donation programs to be able to have a child. After years of intense work, a new IVF technique has been developed, named spindle transfer, that allows the replacement of the entire cytoplasm of poor-quality eggs. This procedure is based on transferring the nucleus (containing the genetic material) of the egg from an affected woman, into donor eggs with a healthy cytoplasm which had their nucleus removed. The eggs resulting from the procedure with the repaired cytoplasm can then be inseminated by conventional techniques (ICSI) with the sperm of the patient's partner, giving the intended parents a chance of having a child genetically related to them. Studies in animals and in human donor eggs donated for research have shown the potential of this technique for the treatment of infertility. The aim of this study is to assess the feasibility of using the spindle transfer technique in patients with poor egg quality undergoing assisted reproductive treatments.

Who can participate?
Women under 40 years old, diagnosed with infertility problems due to poor egg quality, who have had at least two previous failed IVF attempts with or without embryo transfer

What does the study involve?
Participants undergo standard IVF cycle procedures with standard ovarian stimulation. The collected eggs are treated with spindle transfer, inseminated with the patient's partner's sperm, and screened using advanced genetic methods. Those with the correct number of chromosomes are transferred to the patient's womb. Patients who get pregnant are followed up until delivery and the newborns checked up regularly by paediatricians.

What are the possible benefits and risks of participating?
Participants have the opportunity of being treated with a new IVF procedure that may improve the quality of their eggs and increase their chances of pregnancy and having a baby genetically related to them. If there is no pregnancy, patients are offered the possibility of repeating the cycle or being transferred with embryos produced from non-treated donor eggs. Patients are told that this is a pilot study and, despite animal and human research showing evidence of the safety and effectiveness of the procedures, risks are difficult to specify because of the novelty of the treatment. Moving from research into clinical practice always involves some uncertainty. Assisted reproduction techniques that today are routine in IVF laboratories all involved a degree of uncertainty when they were first performed in humans. Scientific reviews convened by the British Human Fertilisation and Embryology Authority (HFEA) have also come to the conclusion that there is no compelling reason to think that cytoplasm/mitochondrial replacement techniques, like spindle transfer, are unsafe. In order to reduce risks as much as possible the patients are monitored after the treatment.

Where is the study run from?
The Institute of Life – IOLIFE, Athens (Greece)

When is the study starting and how long is it expected to run for?
May 2017 to May 2020

Who is funding the study?
The Institute of Life – IOLIFE, Athens (Greece)

Who is the main contact?
Dr Konstantino Kostaras and Dr Panagiotis Psathas
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Study website
http://www.iolife.eu/

Contact information

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Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
ET.IL.LI.003

Study information

Scientific Title
Spindle transfer for the treatment of infertility problems associated to poor egg quality: a pilot trial

Acronym
Cytoplasm donation (CytoDon)

Study objectives
Can spindle transfer enhance the potential of oocytes with limited embryo developmental competence?

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Greek National Authority of Assisted Reproduction, 23/09/2016, No. 437
2. IRB of the IASO Maternity Hospital, 25/05/2017, ref: 2017-001

Study design
Interventional pilot study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Infertility problems associated to impaired embryo development attributed to poor oocyte quality that cannot be overcome with conventional assisted reproduction techniques

Interventions
Infertile patients will undergo through a standard in-vitro fertilization cycle with standard follicular stimulation and oocyte pick-up procedures. The collected oocytes from the patient will then be processed by spindle transfer. This procedure will consist on replacing the cytoplasm of the patient's oocytes by transferring their meiotic spindle into an enucleated oocyte from a donor. After reconstruction, oocytes from spindle transfer and surplus non-manipulated oocytes from the donor will be inseminated with sperm from the patient's couple and cultured in-vitro up to the blastocyst stage. At this moment, the blastocysts from spindle transfer will be biopsied and the samples processed for aneuploidy screening and mtDNA carryover levels. All blastocysts from spindle transfer and controls will be vitrified. Blastocysts from spindle transfer diagnosed as euploid will be warmed and transferred to the patients. After transfer, patients will be followed up until delivery and the newborns checked up regularly by pediatricians.

Intervention Type
Procedure/Surgery

Primary outcome measure
1. Blastocyst formation rates evaluated 5/6 days after the egg pickup using a timelapse incubator to monitor the entire embryo development of each embryo until reaching this stage without disturbing the culture conditions
2. Clinical pregnancies and implantation rates judged by elevation of hCG levels and ultrasound confirmation of a gestational sac by 2/3 weeks after embryo transfer. Pregnancies will be further confirmed 2/3 weeks later with fetal heartbeat

Secondary outcome measures
1. Fertilization judged on the next day of the egg pickup and morphokinetic events associated with embryo development evaluated daily during the following 5/6 days of embryo culture in a timelapse incubator
2. Aneuploidy rates judged in biopsied cells from the blastocysts obtained by spindle transfer and measured using advanced genetic molecular tests for screening the chromosome numbers a few days after the blastocyst biopsy
3. Miscarriage and delivery rates calculated based on the total number of patients that will be diagnosed to be pregnant following the criteria described in the primary outcome

Overall study start date
25/05/2017

Completion date
01/05/2038

Eligibility

Key inclusion criteria
1. Women under 40 years old
2. Diagnosed with infertility problems associated to impaired embryo development attributed to poor oocyte quality

3. At least two previous in-vitro fertilization (IVF) failed attempts with or without embryo transfer

Participant type(s)
Patient

Age group
Adult

Upper age limit
40 Years

Sex
Female

Target number of participants
25 patients

Total final enrolment
25

Key exclusion criteria
1. Women over 40 years old
2. Couples diagnosed with severe male factor infertility

Date of first enrolment
22/02/2018

Date of final enrolment
10/12/2019

Locations

Countries of recruitment
Greece

Study participating centre
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Sponsor type
Hospital/treatment centre

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Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Institute of Life

Results and Publications

Publication and dissemination plan
The study protocol, statistical analysis and experimental design will be available after finishing the trial and submitting the results to a reviewed journal. Planned publication of the results in a high-impact peer reviewed journal.

Intention to publish date
31/10/2021

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Results article	Technical feasibility of maternal spindle transfer	12/02/2023	15/02/2023	Yes	No