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In vitro culture and transfer of human embryos

Submission date
06/04/2016

Recruitment status
No longer recruiting

Registration date
21/04/2016

Overall study status
Completed

Last Edited
19/05/2023

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Assisted reproductive technology (ART) is a group of methods that are used to help infertile couples. For example, during in vitro fertilisation (IVF), eggs are removed from a woman's body and mixed with sperm to make embryos, which are then put back into the woman's body. Intra-cytoplasmic sperm injection (ICSI) differs from conventional IVF in that a single sperm is injected directly into an egg. In natural conditions the egg and embryo are subjected to ever changing dynamic processes. However, routine ART today involve the use of static in vitro culture systems. The aim of this study is to determine whether there is any difference in the viability of embryos after in vitro culture under static and mechanical micro-vibration conditions.

Who can participate?
Woman aged from 23 to 44 years with infertility

What does the study involve?
The woman’s eggs are retrieved and inseminated with her partner’s sperm through conventional IVF and ICSI techniques. Couples are offered the choice of either standard routine culture of the eggs and embryos, or culture with mechanical agitation (micro-vibration) of the culture medium. Embryo development rates are assessed on the day of transfer (Day 2, Day 3 or Day 5).

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Endokrinologikum Ulm, Praxisklinik Frauenstraße (Germany)

When is the study starting and how long is it expected to run for?
January 2010 to December 2015

Who is funding the study?
Cologne University (Germany)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
In vitro culture and transfer of 9,624 embryos from 4,435 patients: micro-vibration increases baby-take-home rate

Study objectives
In natural conditions the egg and embryo are subjected to ever changing dynamic processes. However, the routine assisted reproductive technologies today involve the use of static in vitro culture systems. The objective was to determine whether there is any difference in the viability of embryos after in vitro culture under static and mechanical micro-vibration condition.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Ethical Commissions of Medical Faculties of universities Ulm (12/11/2011, permission 321 /10-UBB/bal) and Cologne (20/11/2013, permission 13-147)

Study design
Observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
In vitro fertilization

Interventions
Patients with infertility were stimulated for in vitro fertilization-cycle (IVF) or intracytoplasmic spermatozoa injection-cycle (ICSI) with triptorelin (Decapeptyl®, Ferring, Kiel, Germany) and recombinant FSH (Puregon®, MSD Sharp & Dohme GmbH, Haar, Germany or Menogon®, MerckSerono GmbH, Darmstadt, Germany or Gonal-f®, MerckSerono GmbH, Darmstadt, Germany) according to the "short" protocol. Ovulation was induced by the administration of 5000 IU of HCG (Brevactid®, Ferring GmbH, Kiel, Germany) and oocytes were retrieved 34 – 36 hours later and inseminated with the partner’s sperm through conventional IVF and ICSI techniques.

Couples were offered the choice of the in-vitro culture of oocytes and embryos according to the standard routine or with mechanical agitation (micro-vibration) until transplantation. Written informed consent was obtained from all the participating couples.

Only two embryos per patient were cultured, as according to German law no more than three pronuclear oocytes/embryos from one patient (usually two) can be cultured in vitro and all cultured oocytes/embryos must be later transferred to the patient independently of the developmental rate of these embryos.

Oocytes for the culture of pronuclear embryos were obtained from 4435 informed patients aged 26–46 years (median age 32.8). Pronuclear embryos (two per patient) were cultured in vitro under two different conditions: Group 1 (n = 4821), without mechanical agitation of the culture medium (standard routine conditions); and Group 2 (n = 4803), with mechanical agitation (44 Hz delivered over 5 s once every hour and acceleration (660 mV/g at 3.3 V: X = ±1.0g, Y = ±0.7g, Z = ±0.15g)).

Mechanical agitation was achieved using the newly developed device Viboviduct 1500 (SimSoTec GmbH, Cologne, Germany, www.vibration-oviduct.com). This device before using was calibrated by measurement of vibration with a special device PCE-VT 2700 (PCE Instruments UK Ltd., Southampton, U.K.). Viboviduct 1500 generates micro-vibrations with a special electric motor with low electromagnetic noise. The generated vibrations are forwarded directly to the plate with Petri dishes. Harmful high frequencies are damped and smoothed by the intelligent control

software developed on the microprocessor. The control software monitors the motor movements. Petri dishes with embryos are fixed on the plate. The device is designed and developed for use in a CO2 incubator.

Embryo development rates were determined on the day of transfer (Day 2, Day 3 or Day 5). The embryos were cultured in 50 µl of culture medium (Sage, Los Angeles, CA, USA) under mineral oil (Sigma, St. Louis, MO, USA) for their transfer.

The embryo on Day 2 and 3 quality system used to grade of the embryos was described by Steer et al. as follows: Grade A, equal sized symmetrical blastomeres; Grade B, uneven blastomeres with < 10 % fragmentation; Grade C, 10 - 50 % blastomeric fragmentation; and Grade D, > 50 % blastomeric fragmentation. Day 5 embryos were graded according to Veeck and Zaninovic.

Embryo transfer (one to three embryos per patient) was performed on Day 2, Day 3, or Day 5 after retrieval of oocytes. Pregnancy was defined as an increase in serum hCG concentration (20 IU/L) determined on 11 and 13 – 15 days after embryo transfer. Clinical pregnancy was recorded when the fetal sac was visualized on an ultrasound on gestational weeks seven to eight.

Intervention Type
Procedure/Surgery

Primary outcome measure
Embryo development rates determined on the day of transfer (Day 2, Day 3 or Day 5)

Secondary outcome measures
N/A

Overall study start date
01/01/2010

Completion date
01/12/2015

Eligibility

Key inclusion criteria
Woman age from 23 to 44 years with infertility

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
4,435

Total final enrolment
4435

Key exclusion criteria
The wish of the patient

Date of first enrolment
04/01/2010

Date of final enrolment
16/12/2015

Locations

Countries of recruitment
Germany

Study participating centre
Endokrinologikum Ulm, Praxisklinik Frauenstraße
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Sponsor type
Research organisation

ROR
https://ror.org/05mxhda18

Funder(s)

Funder type
University/education

Funder Name
Cologne University (Germany)

Results and Publications

Publication and dissemination plan
The manuscript has been submitted for publication

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/06/2017	30/11/2020	Yes	No
Results article		09/05/2017	19/05/2023	Yes	No