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A multicentre randomised controlled trial comparing in vitro maturation of oocytes with in vitro fertilisation in women with an increased risk of ovarian hyperstimulation syndrome.

Submission date
01/03/2010

Recruitment status
No longer recruiting

Registration date
27/05/2010

Overall study status
Completed

Last Edited
27/05/2010

Condition category
Pregnancy and Childbirth

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.studies-obsgyn.nl/ivm

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
NL29051.000.09

Study information

Scientific Title
Comparing in vitro maturation of oocytes with in vitro fertilisation in women with an increased risk of ovarian hyperstimulation syndrome: A multicentre randomised controlled trial with non-randomised pilot study.

Acronym
IVM-study

Study objectives
A randomised controlled trial to compare the following strategies: two In Vitro Maturation - Intracytoplasmic Sperm Injection (IVM-ICSI) cycles or one Controlled Ovarian Hyperstimulation - In Vitro Fertilisation / ICSI (COH-IVF/ICSI) cycle. These strategies are expected to have comparable outcomes for ongoing pregnancy rates and direct costs (treatment costs). IVM is expected to have favourable outcomes for indirect costs (less complications) and quality of life scores.
Our hypothesis is the non-inferiority of the IVM-ICSI strategy to the COH-IVF or COH-ICSI strategy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the Central Committee on Research involving Human Subjects on the 3rd of December 2009 (NL29051.000.09).

Study design
Multicentre randomised active controlled parallel group trial with non-randomised pilot study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Infertility; Polycystic Ovarian Syndrome (PCOS); Ovarian Hyperstimulation Syndrome (OHSS)

Interventions
Patients will be randomised to:

1. IVM/ICSI strategy
1.1. The maximum number of IVM cycles per patient is two.
1.2. The IVM cycle will be sonographically and endocrinologically monitored (serum estradiol concentration).
1.3. In patients with severe oligomenorrhoea or amenorrhoea priming of the ovaries can be performed (after induction of withdrawal bleeding with 7 days 10mg progestogens orally, if necessary).
1.4. Ovarian priming consists of subcutaneous administration of 150IE rFSH on cycle days 3 through 5.
1.5. In primed cycles 10.000 IE of hCG will be administered subcutaneously when the dominant follicle is identified. Oocyte retrieval is scheduled 38 hours after administration of hCG.
1.6. Directly after oocyte retrieval luteal support is started by Estradiol 2 mg orally three times a day and Progesterone 200 mg vaginally three times a day from oocyte retrieval plus one day.
1.7. A maximum number of two embryos will be transferred per cycle. Remaining embryos can be selected for cryopreservation according to the standard IVF/ICSI procedures and criteria.

2. IVF/ICSI strategy
2.1. The maximum number of IVF/ICSI cycles per patient is one.
2.2. After pre-treatment with an oral contraceptive pill or induction of withdrawal bleeding with 7 days 10mg progestogens orally, COH will be started from the 4th day after the end of pre-treatment with daily subcutaneous injections with 100-225 EH rFSH. From stimulation day 6 onwards a GnRH antagonist (0,25 mg) will be daily injected subcutaneously for pituitary down regulation.
2.3. The cycle will be sonographically monitored starting at day 3 after stopping oral contraception (baseline ultrasound). When acquired numbers and diameters of follicles are reached 10.000 IE of hCG is administered subcutaneously and oocyte retrieval scheduled for 34-36 hours after hCG. After oocyte retrieval standard IVF or ICSI procedure will follow.
2.4. Directly after oocyte retrieval luteal support is started by administration of Progesterone 200 mg vaginally two times a day a day.
2.5. The maximum number of embryos that can be transferred is two. Remaining embryos can be selected for cryopreservation according to standard IVF/ICSI procedures and criteria.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
Cumulative live birth rate after IVM/ICSI or COH/IVF/ICSI strategy including pregnancies from cryoembryos transferred within 12 months after the end of IVM/ICSI or COH/IVF/ICSI treatment.

Secondary outcome measures

1. Pregnancy/Childbirth:
Detailed information on maternal complications will be obtained from the obstetrician treating the woman concerned. Six weeks after the expected day of delivery all women will be contacted by telephone to ask information on the delivery and on the health of the child, and for consent to contact the health centre where she gave birth. If a child has been hospitalised the paediatrician treating the child will be contacted for further information.
2. Paediatric follow up:
Follow up will consist of evaluation on the following domains using internationally accredited and validated tests: motor development, cognitive development, and behaviour.
Follow up visits will be scheduled at ages of 6 months, 1, 2, and 5 years.
3. Economic evaluation:
A distinction will be made between costs of medical interventions (direct costs) and costs resulting from productivity losses (indirect or time costs). Standardised unit costs will be calculated for all centres based on actual expenses made during the study. Subsequently, unit costs will be applied to resource use as observed in the participating centres.
Resource utilisation will be documented using individual patient data in the case record forms. In addition, each woman will receive a questionnaire for details on associated direct costs of professional care, and on indirect costs like transportation and productivity loss. These questionnaires will be sent 4 weeks, 12 weeks, 24 weeks and 48 weeks after treatment start.
Resource unit prices will reflect the unit of staff, materials, equipment, housing, depreciation, and overhead. End point for cost-effectiveness will be Euros/live-birth for either strategy.
4. Patient quality of life study:
Before starting a treatment cycle, the day before oocyte retrieval and the day after oocyte retrieval and 3 weeks after a treatment cycle patients will be asked to fill out a validated questionnaire on quality of life (Fertiqol questionnaire, www.fertiqol.org).

Overall study start date
01/01/2010

Completion date
30/09/2012

Eligibility

Key inclusion criteria
1. Women with Polycystic Ovarian Syndrome (PCOS) according to the Rotterdam Criteria (The Rotterdam
European Society of Human Reproduction and Embryology [ESHRE] /American Society for Reproductive Medicine [ASRM] - Sponsored PCOS consensus workshop group, 2004) which not did achieve an ongoing pregnancy after ovulation induction (with clomiphene citrate or Laparoscopic Electrocoagulation of the Ovaries (LEO) and Recombinant Follicle Stimulating Hormone [rFSH])
2. Women with an IVF or ICSI indication and increased risk for developing Ovarian Hyperstimulation Syndrome (OHSS) (history of OHSS or cycle cancellation for imminent OHSS)

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
450 (400 couples, preceded by a pilot study of 50 non-randomised IVM cycles)

Key exclusion criteria
1. Woman or partner younger than 18 years and woman older than 38 years
2. Unable to speak or read the Dutch language
3. Medical contraindication for pregnancy or childbirth
4. Positive serology for Hepatitis B, C or HIV
5. Diminished ovarian reserve: early follicular serum FSH > 10 IU/l and/or poor response during earlier COH/IVF or COH/ICSI with ≥ 150 IU rFSH/day
6. Persisting ovarian cysts > 30 mm diameter

Date of first enrolment
01/01/2010

Date of final enrolment
30/09/2012

Locations

Countries of recruitment
Netherlands

Study participating centre
Jeroen Bosch Hospital
's Hertogenbosch
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5200 ME

Sponsor information

Organisation
Jeroen Bosch Hospital (Netherlands)

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04rr42t68

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Jeroen Bosch Hospital (Netherlands) - Centre for Reproductive Medicine

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration