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Controlled ovarian stimulation and intrauterine insemination or in vitro-fertilisation for the first line treatment of unexplained infertility

Submission date
15/06/2013

Recruitment status
No longer recruiting

Registration date
08/08/2013

Overall study status
Completed

Last Edited
17/05/2017

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
Both intrauterine insemination (IUI) and in vitro fertilization (IVF) are accepted treatment options for unexplained infertility. The recent National Institute for Health and Care Excellence (NICE) guideline proposes to offer IVF as a first-line treatment to these couples excluding IUI. There is no strong evidence on which this recommendation is made, so we aim to conduct this trial of IUI compared to IVF as the first-line management for unexplained infertility. If the live birth rates in both the groups are found to be same, then these couples should not be denied IUI, which is less invasive and more acceptable to patients.

Who can participate?
Couples (with female partner <37 years), trying to conceive for at least a year of unprotected intercourse, in the presence of normal semen analysis, evidence of regular ovulation, open fallopian tubes, and who had no previous fertility treatment other than clomiphene citrate.

What does the study involve?
Couples are randomly allocated to either receive controlled ovarian hyperstimulation (COH) + IUI (50% of women) or IVF (50% of women) as the first offered treatment. The medicines used in the cycles are the same as usual. One cycle of treatment to which the couple is allocated is given in a 12-month period. If they are in the COH + IUI group and fail to conceive in the three cycles then they are automatically recommended for IVF treatment outside of this study. If they are in the IVF group, then after three cycles they are not offered IUI. This is the normal unit policy. The results in the two groups are compared in order to see which group has a better outcome in terms of ongoing pregnancy rate/live birth rate.

What are the possible benefits and risks of participating?
The results of this study will help improve the treatment of people with unexplained infertility in future. There are no added disadvantages and risks over and above the routine treatment.

Where is the study run from?
The study will be carried out in Homerton fertility unit.

When is the study starting and how long is it expected to run for?
The study started in July 2013 and will run for a year or 18 months.

Who is funding the study?
No extra funding is required for this study. Patients' IVF treatment is usually funded by their primary care trust irrespective of their involvement in the study. No extra funding is available.

Who is the main contact?
Dr Anupa Nandi

Contact information

Type(s)
Scientific

Contact name
Dr Anupa Nandi

Contact details
Homerton Fertility Unit
Homerton Hospital
London
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Version no. 2.0

Study information

Scientific Title
Controlled ovarian stimulation and intrauterine insemination or in vitro fertilization for the first line treatment of unexplained infertility: a randomised controlled trial

Study objectives
What should be the first line treatment option for couples with unexplained infertility: intrauterine insemination (IUI) or in vitro fertilization (IVF)?

Ethics approval required
Old ethics approval format

Ethics approval(s)

Brent Ethics Committee, 28/05/2013, ref: 13/LO/0550

Study design
Single-centre randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Best first line treatment options for unexplained infertility

Interventions
Randomisation will be performed by an independent worker in blocks of 10 and distributed in individual consecutively numbered opaque envelopes. Participants will be randomised into two groups:

Group 1: Controlled ovarian hyperstimulation (COH)+ IUI
In COH + IUI group the controlled ovarian hyperstimulation can be performed with daily subcutaneous injections of 75 IU FSH (Fostimon) starting from day 3-4 of menstrual cycle onwards. Dose might be altered according to the response of the patient to be decided by the attending clinician. The follicular growth is strictly monitored by transvaginal ultrasound. When at least 1-2 follicles with diameter 17-18mm is present, final oocyte maturation is induced by administration of recombinant chorionic gonadotropin (hCG) (Ovitrelle) and 24 36 hours later IUI would be performed. If >= 3 follicles of > 16mm develop then the cycle would be cancelled by withholding hCG and IUI and avoiding sexual intercourse due to risk of multiple pregnancies. Semen samples would be processed within one hour of ejaculation using density gradient centrifugation followed by washing with culture medium and then used for insemination. Single insemination will be done

Group 2: IVF
In IVF group women will undergo controlled ovarian hyperstimulation after down-regulation with GnRH agonist in a long protocol starting on day 2. COH is started with FSH (either Menopur or Gonal F) with dose ranging from 150 450 IU depending on initial AMH level decided by the attending clinician. Follicular tracking by transvaginal ultrasound will be performed. Treatment will be continued until follicles are > 18 mm. Ovulation is induced by hCG (Ovitrelle) and cumulus-oocyte complexes will be retrieved by transvaginal ultrasound guided oocyte retrieval 36 hours after hCG trigger. Embryos will be assessed daily for their morphological grading according to our laboratory's protocol until the time of transfer. Day of embryo transfer will be decided by the embryologist based on the embryo quality. One embryo will be transferred on either day 2

or 3 or 5 if one or more good quality embryos are available. If no good quality embryos are available then two embryos will be transferred. Luteal phase support will be provided with progesterone vaginal pessaries (Cyclogest). Non-transferred good quality embryos will be cryo-preserved. In case of unsuccessful cycle or early miscarriage, frozen embryos will be thawed and transferred and this will be counted as another cycle.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Singleton live birth rate is assessed using medical record review

Secondary outcome measures
1. Clinical pregnancy rate is assessed using medical record review
2. Multiple pregnancy rates is assessed using medical record review

Overall study start date
01/10/2012

Completion date
04/08/2016

Eligibility

Key inclusion criteria
1. Couples with female partner's age between 23- 37 years
2. Diagnosed with unexplained infertility at the time of first treatment
3. Inability to conceive following a minimum of one year of unprotected intercourse
4. In the presence of normal semen analysis, proof of regular ovulatory cycles with a day 3 follicle stimulating hormone (FSH)<10IU/L
5. Two patent tubes and a normal uterine cavity on hysterosalpingography (HSG)

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
160 in each group.

Key exclusion criteria
1. Female partner aged 37 years or more
2. People with physical disability or psychosexual problems who find difficulty in achieving

vaginal intercourse
3. Couples in a same sex relationship (as these do not fall into the definition of unexplained infertility)
4. Couples where the male/female is HIV positive, as they would need specific consideration to methods of conception
5. Couples who have had no previous IUI or IVF treatment for infertility

Date of first enrolment
10/08/2013

Date of final enrolment
15/07/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Homerton Fertility Unit
London
United Kingdom
E9 6SR

Sponsor information

Organisation
Homerton University Hospital (UK)

Sponsor details
c/o Mr Narendra Aladangady
R&D Department
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United Kingdom
E9 6SR

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00x444s43

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Patients IVF treatment is usually funded by their primary care trust irrespective of their involvement in the study.

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal.

Intention to publish date
31/12/2017

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from anupa.nandi@gmail.com

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version V4	10/08/2013	15/12/2016	No	Yes
Results article	results	01/06/2017		Yes	No
HRA research summary			28/06/2023	No	No