ISRCTN35880386 https://doi.org/10.1186/ISRCTN35880386

Management of endometriotic ovarian cyst before in vitro fertilisation (IVF)

Submission date	Recruitment status	[_] Prospectively registered
04/12/2007	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
27/03/2008	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
27/04/2016	Urological and Genital Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Tarek Gelbaya

Contact details
Department of Reproductive Medicine
Saint Mary's Hospital
Whitworth Park
Manchester
United Kingdom
M13 0JH
-
tarek.gelbaia@cmmc.nhs.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Management of endometrioma in asymptomatic subfertile patients prior to in vitro fertilisation (IVF)/intracytoplasmic sperm injection (ICSI): a multicentre randomised controlled trial

Study objectives
Surgical removal of endometrioma reduce ovarian response to stimulation during in vitro fertilisation (IVF).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Cumbria and Lancashire B Research Ethics Committee, 10/02/2008, ref: 08/H1016/4

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Endometrioma

Interventions
A total of 40 women with unilateral or bilateral endometriomas who are on the NHS waiting list for IVF will be included in the study. Central randomisation will be employed and one of the investigators will coordinate the process. To avoid any bias, this investigator will not be involved in patients' recruitment or assessment of the outcomes.

Recruitment and treatment allocation:
A fertility specialist will see the patient in the clinic. He/she will explain the study in detail to the patient and then give her an information sheet and a consent form to take home and discuss with others if she wishes. Written informed consent has to be given before entering the trial. Link workers should be made available for those patients whose first language is not English.

If the patient decided not to participate in the study she would simply ring her fertility specialist's secretary and request either to be listed for surgical removal of endometrioma, (a

clinic appointment will be sent for the preoperative check and consenting a week before the operation) or not to have any surgery. In both cases the patient will be seen at Saint Mary's Hospital when she is ready to start her IVF treatment.

If the patient agrees to enter the study, she would simply ring the nursing staff at the IVF unit at St. Mary's Hospital, Manchester, to make an appointment in order to see one of the investigators on day two of her period. During this appointment, the baseline assessment will be completed, and all inclusion/exclusion criteria checked. A research consent form will then be signed by the patient. After consent is obtained, a transvaginal sonography (TVS) will be performed to confirm diagnosis of endometrioma, rule out other pelvic pathology and check antral follicle count (AFC). A blood sample will also be taken on the same day to check follicle stimulating hormone (FSH) and anti-muellerian hormone (AMH).

After the patient has left the clinic the central allocation person will be contacted and the patient allocated to the treatment arm. A referral letters will be sent to the patients and their GP and treating consultant Gynaecologist to inform them of the allocated treatment.

Baseline assessment:
1. Full history taking from the woman and her husband/partner, including details of previous fertility treatment if any
2. Check date and result of the last cervical smear test
3. General examination including weight, height, body mass index (BMI), blood pressure (BP) and urine examination
4. Breast examination (routine examination before IVF treatment)
5. Abdominal examination

Study interventions:
Surgical excision or conservative management of endometrioma prior to COH for IVF.

Surgical approach:
In order to standardise the surgical technique for all the patients, the following should be agreed:
1. Excision of the cyst wall (cystectomy) should be performed with minimal use of diathermy
2. If more than one endometriomas are found at laparoscopy or laparotomy, only endometriomas larger than 3 cm will be removed
3. The procedure can be performed laparoscopically or via laparotomy
4. The procedure will be carried out by a surgeon who is known to do this procedure routinely in his practice and who is employed by one of the six participating centres

COH protocol:
Recombinant FSH (Follitropin beta, Puregon, Organon Laboratories Ltd, Cambridge, UK) will be administered subcutaneously (sc) on day two of spontaneous menstrual cycle in a dose of 150 or 300 IU (depending on the woman's age and the presence of PCOS, not PCO only). The dose will be fixed for the first eight days of ovarian stimulation but may be reduced thereafter depending on ovarian response. Gonadotropin releasing hormone (GnRH)-antagonist (Ganirelix, Orgalutran, Organon Laboratories Ltd, Cambridge, UK) will be administered sc in a dose of 250 micrograms, starting from day six of ovarian stimulation until the day of human chorionic gonadotropin (hCG) administration. Transvaginal ultrasound scan will be performed to monitor follicular growth starting from day eight and every other day until hCG administration. Human chorionic gonadotropin (hCG, pregnyl, Organon Laboratories Ltd, Cambridge, UK) in a dose of 5000 IU will be administered sc if at least three mature follicles (17 mm or larger in diameter) are seen on TVS. Ultrasound guided oocyte retrieval (USOR) will be carried out 34 - 36 hours following hCG

administration. Embryo transfer will be carried out on day two or three after oocytes retrieval. A maximum of two embryos will be transferred at any one time. Vaginal progesterone pessaries (cyclogest, Alpharma) 400 mg twice daily will be prescribed from the day of embryo transfer for two consecutive weeks when a urine pregnancy test will be performed. If pregnancy test is positive, a TVS will be arranged two weeks later to confirm viability and check the number of gestational sacs.

Sample size:
There is little information on which to base a formal sample size estimate. The study has been designed as an exploratory study. A sample size of 20 per arm has been chosen on the basis of feasibility. Allowing for some loss to follow-up, 17 evaluable participants per arm will give an 80% power to detect a large difference of 1 SD in the standardised effects (two-sided t-test at 5% level). It is unlikely, but possible, that there will be differences as large as this, but this study will then give the necessary information to design a definitive study. Results will be presented as effect sizes with associated 95% CI and negative results will not be interpreted as a lack of effect.

Data collection:
The clinician or the local study coordinator will complete a case report form. The completed forms identified by patient's initials, NHS number and centre's initials will be sent by post to the main centre. Data will then be entered into an excel database by the principal investigator at Saint Mary's Hospital.

Statistical analysis:
All analysis will be performed on an intention to treat (ITT) basis. After appropriate transformation, primary and secondary outcomes will be compared between groups using analysis of covariance, adjusting for centre, age and baseline values using appropriate generalised linear models. Results will be reported as mean effects with 95% confidence intervals. Exploratory analyses will investigate the importance of surgeon effects and estimates will be made of the therapist ICC to inform future trials. A p value of greater than 0.05 will be considered statistically significant. No formal adjustments will be made for multiplicity, but this will be taken into account in the interpretation of the results. The detailed analysis plan will be agreed with the Steering Committee prior to the breaking of the blinding.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
1. Serum level of FSH and anti-muellerian hormone (AMH) and antral follicle count (AFC) using transvaginal sonography (TVS) on day two of a spontaneous menstrual cycle before intervention (conservative or surgical management of endometrioma six months or less before IVF cycle) and after intervention (immediately before starting COH for IVF cycle)
2. Duration of gonadotropin (FSH) stimulation (days) and number of FSH ampoules used
3. Number of follicles greater than or equal to 15 mm on the day of human chorionic gonadotropin (hCG) administration
4. Number of oocytes retrieved (oocyte retrieval performed by the same operator)

Secondary outcome measures

1. Number of oocytes fertilised
2. Number of day two embryos available after oocyte retrieval
3. Number of frozen embryos
4. Clinical pregnancy and live birth rates

Overall study start date
01/01/2008

Completion date
31/12/2009

Eligibility

Key inclusion criteria
1. Ultrasonographic findings of unilateral or bilateral endometrioma measuring greater than or equal to 3 cm in diameter, within six months of commencing IVF treatment
2. Women less than or equal to 40 years

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
40

Key exclusion criteria
1. Previous tubal or ovarian surgery (uni- or bi-lateral, including treatment of ectopic pregnancies)
2. Previous controlled ovarian hyperstimulation (COH) cycle ending in cancellation because of inadequate response or where less than four oocytes were retrieved
3. Previous episode of ovarian hyperstimulation syndrome (OHSS), regardless of the degree
4. Concomitant presence of other (i.e., non-endometriotic) ovarian cyst(s)
5. Day 2 - 3 serum follicle stimulating hormone (FSH) levels greater than 10 mIU/mL
6. Women who received any hormonal treatment within six months before commencing COH

Date of first enrolment
01/01/2008

Date of final enrolment
31/12/2009

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Department of Reproductive Medicine
Manchester
United Kingdom
M13 0JH

Sponsor information

Organisation
Central Manchester and Manchester Children's University Hospitals NHS Trust (UK)

Sponsor details
Research and Development Department
Oxford Road
Manchester
England
United Kingdom
M13 9WL
-
keith.chantler@manchester.ac.uk

Sponsor type
Hospital/treatment centre

Website
http://www.cmmc.nhs.uk/

ROR
https://ror.org/00he80998

Funder(s)

Funder type
Industry

Funder Name
Organon Laboratory Limited (UK)

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results:	01/07/2011		Yes	No