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The effect of administration of white blood cells into the uterus on pregnancy outcome in female infertile patients using in vitro fertilization

Submission date
29/07/2019

Recruitment status
No longer recruiting

Registration date
09/08/2019

Overall study status
Completed

Last Edited
06/12/2021

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
In vitro fertilisation (IVF) is one of several techniques available to help people with fertility problems have a baby. During IVF, an egg is removed from the woman's ovaries and fertilised with sperm in a laboratory. The fertilised egg, called an embryo, is then returned to the woman's womb to grow and develop. Though IVF has been useful, its success rate is still far from satisfactory. Previous studies have shown that the amount of blood vessels (vascularity) and the thickness of the lining of the womb (endometrium) were good predictors of live birth in IVF. Since a thin endometrium limits embryo implantation and a key risk factor for women infertility, efforts have been made to augment endometrium thickness using hormonal manipulation, however, they result in modest improvement of endometrial thickness (ET), vascularity, and subsequent pregnancy rate.

Stem cell therapy is a key new concept for improving endometrium function, especially in refractory cases. Peripheral blood mononuclear cells (PBMCs) are a source of stem cells having the potential to divulge into cells of different types. In the present study, we investigated the safety and efficacy of intrauterine administration of PBMCs in the proliferative phase of endometrial development prior to embryo transfer in patients.

Who can participate?
Women aged 21-45 years, with primary and/or secondary infertility, who had at least 3 failed IVF-FET treatments in the past.

What does the study involve?
Participants will have a small amount of blood taken on day 5 or 6 of their menstrual cycle. This blood will be prepared to extract the PBMCs, which will then be infused into the uterus. After 6 or 7 days, endometrium thickness and vascularity will be assessed. Once the endometrium has reached acceptable thickness, the embryo implantation will be carried out as normal.

What are the possible benefits and risks of participating?
Benefits: Chances of higher rate of pregnancy in infertile women.
There are no risks associated with this study.

Where is the study run from?
Institute of Reproductive Medicine, Kolkata, India

When is the study starting and how long is it expected to run for?
April 2016 to April 2020

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
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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
IRM/IEC/BNC-IHP-51

Study information

Scientific Title
Pregnancy outcome in infertile women following intrauterine administration of peripheral blood mononuclear cells: a prospective study

Study objectives
Peripheral blood mononuclear cells (PBMCs) may be a promising therapy for recurrent implantation failures in female infertile patients

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 07/04/2016, Institute of Reproductive Medicine Ethics Committee (HB-36/A/3, Sector-III, Salt Lake, Kolkata 700106; bncirm@gmail.com; (91)33-23215125-27), ref: IRM/IEC/BNC-IHP-51

Study design
Prospective clinical 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 participant information sheet.

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

Interventions
All women patients included in this study had failed to achieve pregnancy previously after a minimum of three FET attempts using standard IVF procedure. In this study, each patient served as an internal control for autologous PBMC treatment and clinical outcomes were measured in each patient before and after the PBMC treatment.

All patients received estradiol valerate (EV) 6.0 mg daily in divided doses from day 2 of their cycle. The dosage of EV was increased sequentially with a maximum of 12 mg per day depending on the endometrial thickness measured by serial transvaginal ultrasonography (TVS). Intrauterine infusion of PBMCs was done at day 5 or day 6 in patients. 10 ml of patient's blood was collected on day 5-6 of a FET cycle and PBMCs were prepared using Lymphoprep density gradient centrifugation. PMBCs were infused immediately into the uterine cavity using a sterile catheter.

Ultrasound examination of the endometrial thickness was done from day 12 or day 13 of the treatment cycle. Assessment of endometrial vascularity was started when the endometrial thickness had reached 7 mm. Applebaum scoring was done to evaluate the vascularity of the endometrium. Presence of blood flow in Zone 3 or Zone 4 of the endometrium was taken as favourable parameter for frozen embryo transfer. When adequate endometrial preparation was achieved in the treatment cycle in terms of favorable endometrial thickness, morphology, and vascularity, progesterone was administered. FET was done after three days of progesterone administration. Progesterone was continued even after FET for luteal phase support (LPS) and was discontinued once the pregnancy had been confirmed and is producing an adequate amount of progesterone on its own. Human chorionic gonadotropin (hCG) levels were measured 13 days after FET to confirm biochemical pregnancy. The cardiac activity of the fetus was monitored by trans vaginal ultrasound sonography (TVS) after 3 weeks of FET to confirm a viable clinical pregnancy.

Intervention Type
Supplement

Primary outcome measure
1. Pregnancy rate at 12-weeks
2. Miscarriage rate at 12-weeks

Secondary outcome measures
1. Endometrial thickness measured using ultrasound examination at baseline and 12-weeks
2. Endometrial vascularity measured by transvaginal sonography (TVS) and Applabaum scoring was done evaluate the vascularity at baseline and 12-weeks

Overall study start date
15/03/2016

Completion date
30/04/2020

Eligibility

Key inclusion criteria
1. Female
2. Aged 21-45 years
3. Primary and secondary infertility
4. At least 3 failed IVF-FET

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
95

Total final enrolment
95

Key exclusion criteria
1. Adenomyosis
2. Congential uterine anomalies
3. Baseline FSH> 12 IU
4. Donor oocyte recipients
5. Gestational surrogates

Date of first enrolment
16/04/2016

Date of final enrolment
31/12/2018

Locations

Countries of recruitment
India

Study participating centre
Institute of Reproductive Medicine
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Sponsor information

Organisation
Institute of Reproductive Medicine

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/03jgxy838

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
Trial results have been communicated to a peer-reviewed journal.

Intention to publish date
15/08/2019

Individual participant data (IPD) sharing plan

All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/09/2020	06/12/2021	Yes	No