ISRCTN50956936 https://doi.org/10.1186/ISRCTN50956936

PREPARE (PREconcePtional diet in Assisted Reproductive tEchnology): Preconceptional diet and embryo quality

Submission date
10/02/2014

Recruitment status
No longer recruiting

Registration date
10/02/2014

Overall study status
Completed

Last Edited
27/07/2020

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
The Southampton Women's Survey showed that the diet of both men and women can affect their fertility, the health of the pregnancy and the long term wellbeing of the children. Studies suggest that a diet rich in Vitamin D and omega-3 fats might improve the outcome from in vitro fertilisation (IVF) but this idea has not been tested. In this context it is known that some fats are essential for the cells that are required by the lining of the womb to allow it to receive a developing pregnancy. We think that a short period of improved diet in couples wishing to embark on IVF after a prolonged period of subfertility may make a difference to the success of the IVF. Therefore we are conducting this study to test our idea.

Who can participate?
Couples about to undergo IVF will be recruited from the Complete Fertility Centre situated in Princess Anne Hospital, Southampton.

What does the study involve?
The couples will be randomly allocated to the test diet or to the control diet. The test diet will be a daily fruit-based drink high in Vitamin D and omega -3 fats together with standard doses of Vitamin C and folic acid plus olive oil for cooking and olive oil-based spreads. The control diet will be the daily fruit-based drink without added Vitamin D or omega-3 fats but including the Vitamin C and folic acid plus sunflower oil for cooking and sunflower oil-based spreads. The results will be analysed to determine whether the intervention diet improves the quality and number of embryos obtained from the IVF cycle. Differences in the nutrient content of the fluid from the womb and ovaries and of the woman's blood between the two groups will also be examined, as will any change in the man's semen quality. Following IVF, the baby's growth will be measured at 7, 12 and 20 weeks of pregnancy and at birth the baby's birth weight and length will be recorded. In the first few weeks of life the baby's bone density will be measured.

What are the possible risks and benefits of taking part?
There are a number of benefits of taking part in the study. The couple will be provided with a food hamper that may improve their health. An endometrial scratch (taking a sample from the

lining of the womb) will also be carried out; this is thought to increase the chances of success during IVF. Finally, an embryoscope will be used to culture and closely monitor the growing embryos; if the embryo is transferred then the couple will be given a copy of this film. There are no immediate direct risks of participating in the study. Additional samples of fluid and tissue will be taken, the risks of which are negligible.

Where is the study run from?
The study will be conducted from the Complete Fertility Centre, Princess Anne Hospital and the University of Southampton, UK.

When is the study starting and how long is it expected to run for?
Study recruitment will start in February 2014 and continue for about 18 months.

Who is funding the study?
The funding has been received from the NIHR Southampton Biomedical Research Centre in Nutrition and Complete Fertility Centre at the University Hospital Southampton NHS Foundation Trust, UK.

Who is the main contact?
Dr Alexandra Kermack
Alexandra.Kermack@uhs.nhs.uk

Contact information

Type(s)
Scientific

Contact name
Dr Alex Kermack

Contact details
University of Southampton
Obstetrics and Gynaecology (MP 815)
Room F89, Level F
Princess Anne Hospital
Coxford Road
Southampton
United Kingdom
SO16 5YA
-
Alexandra.Kermack@uhs.nhs.uk

Additional identifiers

Protocol serial number
15896

Study information

Scientific Title

A randomised controlled trial of a preconceptional dietary intervention in women undergoing IVF treatment

Acronym
PREPARE

Study objectives
That a specific dietary intervention delivering healthy nutrients started 6 weeks prior to IVF will improve embryo quality and development.

More details can be found at: http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=15896

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee South Central - Oxford A,15/11/2013, ref.:13/SC/0544

Primary study design
Interventional

Study design
Single-centre double-blinded randomised controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Reproductive Health and Childbirth; Subtopic: Reproductive Health and Childbirth (all Subtopics); Disease: Reproductive Health & Childbirth

Interventions
Dietary intervention, The intervention diet consists of a daily supplemented drink high in Vitamin D (10 micrograms) and the omega 3 fatty acids EPA and DHA (2 g daily) together with standard doses of Vitamin C and Folic acid. They will also be asked to use olive oil for cooking and olive oil based spreads.

The control diet consists of a daily supplemented drink (Folic acid and Vitamin C only) with sunflower oil and sunflower oil based spreads.

Intervention Type
Supplement

Primary outcome(s)
Embryo development from zygote to blastocyst stage will be monitored using a validated time-lapse incubator and analysed according to the time of embryo cleavage from two to three cells (CC2).

Key secondary outcome(s)
Other embryo development markers will be analysed including CC3 (the duration of the third cell cycle), S2 (the synchrony in division from two to four cells), T5 (the time of division to 5 cells)

and the time of appearance and disappearance of the pronuclei. These markers have all been demonstrated to be related to embryo quality and hence pregnancy rates.

Other secondary outcomes that will be examined include the changes in nutritional status of blood, uterine fluid and follicular fluid prior to and following the intervention in the control and placebo group. The immune cell populations in the endometrium will also be analysed as previous studies have shown that these may be modulated by local inflammatory mediators, including eicosanoids, the expression of which is dependent on fatty acid substrates. Changes in semen quality and the nutritional content of the sperm and seminal fluid will be assessed and compared between the two groups.

Fertility markers such as number of cleavage stage embryos; number of embryo of sufficient quality for cryopreservation; implantation rates and clinical pregnancy rates will be recorded. In those participants with ongoing pregnancies, antenatal markers will be measured at 7, 12 and 20 weeks by ultrasound scan including fetal crown rump length, head circumference, brain volume, abdominal circumference, femur length, cross sectional distal metaphyseal volume and placental volume.

Perinatal markers (birthweight and length and placental dimensions and weight) will be documented at birth and, in participants who consent, a neonatal DXA to assess bone density will be performed.

Completion date
31/01/2016

Eligibility

Key inclusion criteria
1. Standard indication for IVF/ICSI treatment
2. Female BMI between 20 and 32kg/m2
3. Non-smoker for previous 6 months
4. Good understanding of written and spoken English

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
222

Key exclusion criteria
1. More than two previous unsuccessful IVF cycles
2. Female age >41

3. Anti-mullerian hormone (AMH) less than 7pmol/l or antral follicle count (AFC) less than 10
4. Previously diagnosed diabetes
5. Previous diagnosis of HIV, Hepatitis B or C
6. Any medical contraindication to IVF/ICSI treatment
7. Any medical contraindication to a specific dietary intervention
8. Taking any prescribed medication or herbal remedies apart from simple painkillers
9. Eating oily fish (as defined by the Food Standards Agency) more than once per week

Date of first enrolment
01/02/2014

Date of final enrolment
01/08/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Southampton
Southampton
United Kingdom
SO16 5YA

Sponsor information

Organisation
Southampton University Hospitals NHS Trust (UK)

ROR
https://ror.org/0485axj58

Funder(s)

Funder type
Research organisation

Funder Name

The main funding for the study comes from the NIHR Southampton Biomedical Research Centre (UK) - This is Project 1b of Area 1 of the BRC's research programme.

Funder Name
Some funding will come from Complete Fertility Centre.

Funder Name
Smartfish will provide materials (drinks) at no charge, and Fertilitech will loan us the embryo incubator with time lapse analysis facility.

Results and Publications

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	01/02/2020	27/07/2020	Yes	No
Protocol article	protocol	18/11/2014		Yes	No
HRA research summary			28/06/2023	No	No