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HABSelect: a new sperm selection process for ICSI (Intracytoplasmic Sperm Injection) aimed at increasing live birth outcomes and reducing miscarriage rates

Submission date
08/08/2013

Recruitment status
No longer recruiting

Registration date
08/08/2013

Overall study status
Completed

Last Edited
25/04/2022

Condition category
Pregnancy and Childbirth

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Male infertility accounts for almost half of all referrals to the IVF clinic for assisted conception. In many cases, the male sperm are present but are either unable to fertilise his partner's egg or the embryo fails to implant or even miscarries at a later stage. It is possible to inject sperm directly into the egg [Intracytoplasmic Sperm Injection (ICSI)] and for pregnancies to be achieved as a result. Unfortunately, however, although this method is very often successful at fertilising the egg, achieving a viable pregnancy is far less successful. It is estimated that on average, once transferred to his partner's uterus, less than a quarter of all fertilised eggs will implant and develop into a baby to term. Recently, a new method for sperm selection has been developed and initial results suggest it may help pregnancy outcomes. The method relies on selecting sperm by their ability to stick to a naturally occurring substance hyaluronan that is normally found close to the surface of the egg. This material can be coated on to a special plate and if the male sperm is allowed to swim or flow over the material, the 'best' sperm will bind to the coating and can then be easily picked for injection. This study aims to show that replacing the usual sperm selection step with this method can significantly improve the live birth rate. This study also aims to assess other factors including pregnancy rate, live birth rate and pregnancy loss.

Who can participate?
This study aims to recruit 3730 couples undergoing ICSI treatment, aged over 18 years.

What does the study involve?
Couples will be randomly allocated to one of two groups: the intervention group where the specialists will select the sperm using hyaluronan binding for the ICSI procedure; the control group where they will select the sperm using the standard practice. The group to which the couple are allocated to will be decided by a process called randomisation, which is like a coin toss. The study does not involve any additional procedures, we will only collect the treatment outcomes for all participating females. At the end of the study, we will compare the live birth

rate in both groups. We will also look at the miscarriage rate and clinical pregnancy rate, which reflects how many treated women with embryo(s) transferred into their womb, proceeded to pregnancy confirmed by detecting a fetal heartbeat or fetal sac.

What are the possible benefits and risks of participating?
There will be no immediate direct benefit to those taking part. This research may, however, in time improve general ICSI treatment and its outcome rates. ICSI is routinely performed and as might be expected from a naturally occurring substance that is present throughout the body, there have been no reported risks with using hyaluronan. Hyaluronan-coated plates are already approved for clinical use for that purpose. It means they went under rigorous testing and no risks to patients using them have been described by the manufacturer. There are no other risks.

Where is the study run from?
This study is run from 16 fertility centres across the UK.

When is study starting and how long is it expected to run for?
It is anticipated that recruitment will start in second half of 2013. The total study recruitment period is expected to last for a minimum of 21 months and then follow up will continue till the last pregnancy outcome is known. We plan to complete the study recruitment in 2016.

Who is funding the study?
Funding has been provided by National Institute for Health Research - Efficacy and Mechanisms Evaluation (NIHR-EME) grant, UK.

Who is the main contact?
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Contact information

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Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
14845

Study information

Scientific Title
Selection of sperm for Assisted Reproductive Treatment by prior hyaluronic acid binding (HABSelect): increasing live birth outcomes and reducing miscarriage rates multicentre randomised controlled, blinded trial

Acronym
HABSelect

Study objectives
1. We aim to test the hypothesis that the outcome of current standard treatment for Intracytoplasmic Sperm Injection (ICSI) - an important procedure for fertility treatment - can be potentially improved by deployment of a prior sperm selection step using hyaluronan-coated plates (PICSI). The PICSI plates are thought to select more mature and 'better quality' sperm that can bind to its hyaluronan coating. This method may increase the live birth rate and correspondingly decrease miscarriage rate in pregnancies resulting from ICSI treatment.
2. We also hypothesise that hyaluronan-selected sperm have more efficiently packaged chromatin with lower levels of DNA damage that help support normal embryonic development.

CLINICAL OBJECTIVES:
1. Primary
To determine if hyaluronan-selected, Intracytoplasmic Sperm Injection (PICSI) results in more term (37 or above weeks gestation) live birth deliveries in comparison with the current standard treatment (PVP ICSI).
2. Secondary
To determine the impact on:
2.1. increasing clinical pregnancy rate (CPR) based on detection of fetal heartbeat or presence of fetal sac
2.2. reducing miscarriage rate defined as pregnancy loss after confirmation of clinical pregnancy
2.3. increasing pre-term live birth rate (below 37 weeks' long).

MECHANISTIC OBJECTIVES:
1. Primary
To evaluate if PICSI can compensate for poor sperm quality and investigate how sperm binding to hyaluronan (assessed by testing for hyaluronan binding score - HBS) relates to their genetic material and to live birth rate.
To evaluate the differences in chromatin (genetic material) architecture in ICSI- prepared sperm with high and low hyaluronan binding scores (HBS) including any correlation with DNA damage.

2. Secondary
The primary mechanistic evaluation will be extended to selected sperm samples collected from the density gradient (DGC) interface layer of prepared sperm that is not used for the fertility treatment. We wish specifically to determine the relationship between genetic material packaging and the level of its damage in these interface samples with the HBS of the corresponding pellets used for treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Yorkshire and The Humber REC: Sheffield, 11/06/2013, ref: 13/YH/0162

Study design
Parallel-group two-arm multicentre blinded randomised controlled clinical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Currently not available in web format. Please use the contact details to request for couple information sheet with informed consent form.

Health condition(s) or problem(s) studied
Male-related fertility treatment

Interventions
PICSI - hyaluronan-based sperm selection system has been approved for clinical use but not introduced into wider practice yet.
Hyaluronan is a natural substance in the body and is currently used for different medical and non-medical purposes. It is also found close to the surface of the egg and thought to be involved into process of sperm selection by the egg for subsequent fertilisation.
1. Hyaluronan coated plates (used in the Intervention Group) make use of that hyaluronan property - the coating binds selectively more mature sperm allowing the embryologist or andrologist to easily pick a sperm for injection.
2. The control (non-intervention) group will receive the current standard treatment, where the sperm is visually selected by the embryologist or andrologist.
The participating couples and their clinical team will be blinded to the study allocation as well as research nurses who follow up the pregnancy outcome of participating females. The study will also collect the sperm left (residual) after ICSI treatment. The research team will perform a series of additional tests on these samples looking in more depth at the way genetic material is packaged in the cell and how its damage correlates with the sperms' ability to bind to

hyaluronan and to live birth rate. All the tests performed are established techniques used to research DNA structure and damage in sperm cells.

Intervention Type
Procedure/Surgery

Primary outcome measure
1. Clinical: Live birth at ≥37 weeks' gestation following the first fresh ICSI treatment
2. Mechanism: HBA score will be recorded on the day of PICSI / PVP-ICSI procedure and DGC washed sperm will be examined, retrospectively for disruption of chromatin architecture and DNA damage

Secondary outcome measures
Clinical:
1. Clinical pregnancy rate based on detection of a fetal heartbeat or the presence of fetal sac at 6-9 weeks' gestation
2. Miscarriage, defined as pregnancy loss after confirmation of clinical pregnancy
3. Live birth <37 weeks' gestation

Mechanism: Chromatin disruption in relation to DNA damage and DNA packaging anomalies in 45:90 interface samples and correlation between clinical and post-clinical HBA scores in relation to initial sperm concentration. The relationship between the tests of chromatin and DNA integrity with live birth outcome and miscarriage will be dynamically assessed by statistical modelling

Overall study start date
01/07/2013

Completion date
30/09/2017

Eligibility

Key inclusion criteria
Current exclusion criteria as of 13/01/2015:
1. Couples able to provide informed consent.
2. Couples undergoing first fresh ICSI procedure.
3. Women:
3.1. BMI: 19.0 – 35.0 kg/m2
3.2. FSH level 3.0 – 20.0 miU/ml and/or AMH ≥1.5 pmol/L
3.3. Age: 18 to 43
4. Men:
4.1. Age: 18 to 55
4.2. Able to produce freshly ejaculated sperm for the treatment cycle

Previous exclusion criteria:
1. Couples able to provide informed consent.
2. Couples undergoing first fresh ICSI procedure
3. Women :
3.1. BMI: 19.0-30.0 kg/m2
3.2. Hormonal level: Anti-Mullerian Hormone (AMH) level 0.8 , 2.5 ng/ml and/or Follicle-

Stimulating Hormone (FSH) level 3 , 10 miU/ml
3.3. Age: 18 to 43
4. Men:
4.1. Age: 18 to 55
4.2. Able to produce freshly ejaculated sperm for the treatment cycle

Target Gender: Male & Female; Upper Age Limit 55 years ; Lower Age Limit 18 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 7460; UK Sample Size: 7460 (3730 couples)

Total final enrolment
2772

Key exclusion criteria
Current exclusion criteria as of 13/01/2015:
1. Couples who have not consented prior to ICSI will be ineligible
2. Couples using non-ejaculated sperm
3. Couples using donor gametes
4. Men with vasectomy reversal; cancer treatment involving any chemotherapy and/or radiotherapy in the previous two years
5. Previous participation in the HABSelect trial
6. Split IVF/ICSI
7. If both FSH and AMH are tested and either of them falls outside the accepted range

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Date of first enrolment
17/12/2013

Date of final enrolment
31/08/2016

Locations

Countries of recruitment
United Kingdom

Study participating centre
Assisted Conception Centres at http://www.habselect.org.uk/recruitment-sites/index.html
United Kingdom
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Sponsor information

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ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Government

Funder Name
National Institute of Health Research - Efficacy and Mechanisms Evaluation (NIIHR-EME) Grant: Ref: 11-14-34-Miller

Results and Publications

Publication and dissemination plan

The Trial Steering Committee will agree a publication plan and be consulted prior to release or otherwise publish any study data. We anticipate that in addition to the interim final report required by the funder in September 2017 (open access), all outcomes from the study will be submitted for peer review in the appropriate, open access journals. Communications will also be delivered at key international meetings associated with relevant reproductive societies and groupings. Patients and other stakeholders will also be able to obtain information on their arm allocation after accessing a website that will be set up specifically for this purpose. As per the funder's requirements all materials to be submitted for publication will be sent to the NIHR Coordinating Centre for EME (NCCEMEM) for approval and prior to publication.

All participant-level data will be made available to the scientific community and other interested parties once the database has been closed, cleaned and analysed and steps taken to ensure that all data with respect to patient participation remain confidential and anonymous. The main outcomes of the study reported via the usual peer-reviewed process. On request, patient participants will be able to ask which arm of the study they were in although exactly how we shall implement this service is under discussion.

Intention to publish date

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	07/10/2016		Yes	No
Results article	results	02/02/2019	01/09/2020	Yes	No
Results article		23/04/2022	25/04/2022	Yes	No
HRA research summary			28/06/2023	No	No