ISRCTN77877146 https://doi.org/10.1186/ISRCTN77877146

Effect of chemotherapy and ionising radiation on sperm nuclear and mitochondrial DNA: Can pre-treatment with GnRH Agonists reverse these effects?

Submission date
30/09/2005

Recruitment status
No longer recruiting

Registration date
30/09/2005

Overall study status
Completed

Last Edited
13/03/2014

Condition category
Urological and Genital Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N0265055944

Study information

Scientific Title

Study objectives
1. To examine whether chemotherapy/radiotherapy induced azoospermia/severe oligozoospermia can be reduced or prevented by 'down-regulation' of the pituitary using GnRH agonists.
2. If partial or complete gonadal protection is conferred by GnRH, will the sperm subsequently produced be damaged genetically?
3. If previously impaired sperm production in (due to the nature of the malignancy) improve post protective treatment with GnRHA?
4. To examine the effects of chemotherapeutic agents on sperm nuclear and mitochondrial DNA and the induction of apoptosis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Not Specified

Participant information sheet

Health condition(s) or problem(s) studied
Urological and Genital Diseases

Interventions
The investigations will comprise the following:

Sperm Storage
Immediately on referral, patients will be given the opportunity to have spermatozoa cryopreserved at the ACU, Birmingham Women's Hospital. Briefly, after a full semen analysis

(see below) and completion of relevant documentation, an equal amount of cryoprotectant media is added to the semen over a period of 10-15 minutes. Vials are then suspended in liquid nitrogen vapour.

Semen Analysis
Full semen analysis, including sperm concentration; motility; morphology; antisperm antibodies. vitality are carried out in accordance with the World Health organisation (WHO, 1992). Computer assisted sperm motility analysis (CASA) will also be performed, using an Hamilton Thorn IVOS (version 8.1).(Tomlinson Ct al, 1993).

Blood tests
Bloods for serum FSH and testosterone will be taken at the time of semen analyses.
Sperm nuclear DNA (nDNA) and mitochondrial DNA (mtDNA)
Sperm nuclear DNA Damage will be assessed using the TUNEL assay or using the sperm nuclear clromatin integrity analysed using the Chromomycin A3 fluorochrome (Manicardi et al, 1995; 1998) Mitochondrial DNA fragmentation will be studied using long PCR according to the methods of St.John, (in press).

Mitochondrial Function
Mitochondrial membrane potential will be assessed using the fluorescent probe D1Oc6 counterstained with propidium iodide for sperm viability according to the methods Zamzami et al (1996).

Samples
Samples will be assessed immediately after referral from the oncology centres. A second sample will be assessed 3 months later and then again at 6 months.

All the above mentioned techniques have been developed and validated and are in current use in our laboratories.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
Not provided at time of registration

Secondary outcome measures
Not provided at time of registration

Overall study start date
01/10/2003

Completion date
01/01/2007

Eligibility

Key inclusion criteria

Patients will be referred from tertiary referral centres in Birmingham. These will include principally the Queen Elizabeth Hospital in Edgbaston, Selly Oak Hospital and the Dept of Haematology, Heartlands Hospital. They will have been referred for sperm storage to prior to chemo or radiotherapy mainly in cases of malignant disease but also in other conditions e.g. treatment of nephrotic syndrome. Patients will be randomised to treatment groups at the point of intention to treat.

Participant type(s)
Patient

Age group
Adult

Sex
Male

Target number of participants
Not provided at time of registration

Key exclusion criteria
Not provided at time of registration

Date of first enrolment
01/10/2003

Date of final enrolment
01/01/2007

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Clinical Haematology
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Sponsor information

Organisation
Department of Health

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Sponsor type
Government

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Funder(s)

Funder type
Government

Funder Name
University Hospital Birmingham NHS Trust (UK)

Funder Name
Research Funds

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