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Pilot antioxidant therapy of men in unexplained miscarriage: the pAToMiUM trial

Submission date
15/07/2019

Recruitment status
No longer recruiting

Registration date
05/09/2019

Overall study status
Completed

Last Edited
19/08/2022

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Many couples experience miscarriage, but 1 in 100 couples in the UK experience recurrent miscarriage (defined as three or more miscarriages), which often has no explanation or available treatment. One reason for the lack of explanation is our neglect of detailed examination of the male partner, particularly the causes and effects of sperm with damaged DNA. One reason for the lack of explanation is our neglect of detailed examination of the male partner, particularly the causes and effects of sperm with damaged DNA.
We propose to test the effects of a combined vitamin and mineral supplement in a pilot trial on 30 men with poor sperm DNA quality in our recurrent miscarriage population. We have worked with one of Europe's leading producers of nutritional supplements to design the supplement formulation according to the latest evidence. As the process by which sperm are made takes around 70 days the men will be asked to take the supplement for at least three months with monitoring during this time of sperm DNA quality. While the men are on the supplement and in the successive three months we will also monitor whether the medication increases the chance of a natural pregnancy and whether this pregnancy goes to term. As all components are available to individuals via many different supplements we see no reason to insist that the couples take contraceptive precautions during the pilot trial.
This trial pilot topic was selected after extensive engagement with our patient population, and the study has been designed with their guidance.

Who can participate?
Couples who have had two or more miscarriages in the past

What does the study involve?
The purpose of this study is to test whether a large clinical trial of giving men a specially formulated food supplement 'vitamin pill' is feasible. Participation in our study is entirely voluntary. To make sure the test is fair, participants are split into two groups and neither researchers nor the participants know which group participants are in. The active treatment group take a pill that contains a series of vitamins and minerals that we have specifically chosen to help the DNA in sperm pack better and be less likely to be damaged. This formulation is not available commercially, so it is not available in a pharmacy or online. All ingredients in the pill are common and routinely recommended as part of a healthy diet. People in the control group take

a dummy treatment, which looks identical to active pill, called a placebo. Trials have placebo groups to give us a baseline that we can compare to and see if the treatment has any effect. Participants cannot request to be placed in either group. Participants will provide semen and blood samples for analysis three times in the trial and keep a food diary

What are the possible benefits and risks of participating?
At the moment there is not enough evidence to say whether the trial supplement is beneficial. Minor side-effects of any food supplementation can include an upset stomach, but this is rare. All of the ingredients in our supplement are known to be safe and are common in food.

Where is the study run from?
Tommy's National Miscarriage Centre, Birmingham Women's Hospital, UK

When is the study starting and how long is it expected to run for?
December 2019 to December 2021.

Who is funding the study?
1. National Institute for Health Research (NIHR)
2. Bayer HealthCare

Who is the main contact?
Dr Jackson Kirkman-Brown
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2019-000315-91

Protocol serial number
42663

Study information

Scientific Title
The pAToMiUM trial - pilot Antioxidant Therapy of Men in Unexplained Miscarriage

Acronym
pAToMiUM

Study objectives
Using a minerals and antioxidants dietary supplementation may improve sperm DNA quality, in turn resulting in better reproductive outcomes. This blinded randomised controlled pilot study will assess feasibility of a full-scale trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, East Midlands - Derby Research Ethics Committee (Riverside Centre (Derwent Room), Pride Park, Derby, Riverside Court, Pride Park, Derby, DE24 8HY; +442071048036; NRESCommittee.eastmidlands-derby@nhs.net), ref: 19/EM/0208

Study design
Randomised; Both; Design type: Treatment, Screening, Drug, Physical, Active Monitoring, Validation of investigation /therapeutic procedures

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Miscarriage, elevated sperm DNA fragmentation

Interventions
Menevit is a daily food grade dietary supplementation (oral single-tablet combined vitamin, antioxidant and mineral dietary supplement) designed for men considering conception by BAYER Consumer Health, which will be tested in this double-blinded, placebo-controlled pilot trial.

Participants will be screened into the trial via having elevated sperm DNA fragmentation as measured by the TUNEL assay. Men that are eligible for the study will be randomised to take this supplement or matched placebo.

Men will take the single tablet once daily for 6 months and will provide a semen sample at 1 and ≥3 months post-randomisation. The couple will be followed up for 12 weeks post-supplement cessation to report the outcome of any pregnancy.

Mechanistic testing will include number of semen, antioxidant balance and ROS, sperm chromatin & DNA structure and other relevant assays. Dietary information will also be taken.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
MENEVIT dietary supplement

Primary outcome(s)
Feasibility outcomes:
1. Proportion of screened men that are eligible for the trial on the basis of their baseline sperm sample
2. Proportion of eligible couples randomised
3. Proportion of potentially eligible men who consent to baseline sperm sample provision
4. Proportion of randomised men that return for their 1 month and 3 month follow-up visits for additional sperm sample provision
5. Men's compliance to taking the daily nutritional supplement and reasons for stopping taking the trial intervention early
6. Proportion of couples that withdraw from the trial, and the reasons for this
7. Proportion of couple that are lost to follow-up

Key secondary outcome(s))
1. Mechanistic monitoring
1.1 Amount of sperm DNA damage relative to baseline after 1 month on the trial intervention
1.2 Changes in conventional sperm parameters after 1 month on the trial intervention
1.3 Amount of sperm DNA damage relative to baseline after 3 months on the trial intervention
1.4 Changes in conventional sperm parameters after 3 months on the trial intervention

2. Clinical monitoring
2.1 Ongoing pregnancy at 12 completed weeks of gestation
2.2 Spontaneous conception rates whilst the man is taking the treatment
2.3 Adverse events related to the trial intervention

3. Acceptability and impact on patients (outcome). All men will be requested to complete a short questionnaire at their 3-month follow-up visit to assess:
3.1 How the trial impacted on their day-to-day life, including the attendance of follow-up visits.
3.2 The acceptability of taking the daily nutritional supplement.
3.3 Suggestions for making improvements to the recruitment processes.

Completion date
28/07/2023

Eligibility

Key inclusion criteria

Male participants:
1. Aged 18 or over
2. Two or more previous unexplained miscarriages with their current female partner
3. Currently trying to conceive with their current female partner
4. Willing to provide repeated ejaculated sperm samples for analysis
5. Sperm DNA damage greater than or equal to 20% at baseline (as determined using the Birmingham TUNEL assay)

Female participants:
1. Aged 18 to 40
2. Willing to take folic acid supplement as per medical guidelines, this is not part of the trial and would be expected in routine practice for all patients

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
15

Key exclusion criteria
Male participants:
1. Previous participation in pAToMiUM
2. Current smoker
3. Unwilling to provide repeated ejaculated sperm samples for analysis
4. Evidence for bacterial infection in semen on baseline semen analysis
5. Currently taking dietary supplementation and unwilling to switch to the trial supplement alone
6. Known genetic cause of previous miscarriage (e.g. chromosomal translocation)

Female participants:
1. Participation in any other trial of an investigational medicinal product
2. Female partner is known to be pregnant at the time of randomisation
3. Known genetic cause of previous miscarriage (e.g. chromosomal translocation)

Date of first enrolment
01/12/2019

Date of final enrolment
03/08/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Tommy's National Miscarriage Centre, Birmingham Women's Hospital
Birmingham Women's & Children's NHS Foundation Trust
Mindelsohn Drive
Edgbaston
Birmingham
United Kingdom
B15 2TG

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
NIHR Academy; Grant Codes: Health Care Science SCL-2014-05-001

Funder Name
Bayer HealthCare

Alternative Name(s)
BHC

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during the current study will be available upon request from the Birmingham Clinical Trials Unit at the University of Birmingham in an anonymised format after the trial has been published. Requests for the sharing of data will be reviewed by a Data Sharing Committee

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes