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ORCHARD: Study to prevent progression of kidney disease in pregnancy

Submission date
09/11/2019

Recruitment status
No longer recruiting

Registration date
29/01/2020

Overall study status
Completed

Last Edited
20/05/2024

Condition category
Urological and Genital Diseases

[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
Pregnancy can worsen chronic kidney disease (CKD). Low nitric oxide may stop kidneys coping with pregnancy and by replacing nitrate in the form of a dietary supplement (beetroot juice) we may be able to protect kidney function in pregnancy.

Who can participate?
Pregnant women aged 18 years or above with CKD Stages 2-5

What does the study involve?
This study will recruit pregnant women with CKD to monitor their health during pregnancy and look for any possible associations between those women in whom kidney function worsens during pregnancy and those in who do not have a reduction in kidney function.
Some participants will be asked to drink a beetroot juice supplement daily for the duration of their pregnancy. The study will tell us how many women are willing to take part, how women felt about the trial and whether they were happy to take treatment. We will also look at treatment effects on kidney function and babies' growth and wellbeing. These measurements will be used to plan a bigger study to test whether treatments can protect kidney function in pregnancy.

What are the possible benefits and risks of participating?
Participating in the observational study may benefit pregnant women with kidney disease in the future. The risks of participating in the observational arm are minimal and relate to time and mild discomfort that may be experienced when taking samples (blood, saliva, tongue scraping). Possible benefits of Orchard Beet include lowering of blood pressure and possible reduction in pregnancy associated kidney function decline and pregnancy complications. The risks are that this treatment may lead to hypotension (low blood pressure), may be unpleasant to take and may have unanticipated side effects. The dietary nitrate has been studied in other pregnant and non-pregnant populations and has been well tolerated and associated with very little risk to participants.

Where is the study run from?
King's College Hospital NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
February 2020 to April 2024

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

Who is the main contact?
Dr Kate Bramham
kate.bramham@kcl.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Kate Bramham

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Additional identifiers

Central Portfolio Management System (CPMS)
44456

Protocol serial number
JFS_RP_008_20170915

Study information

Scientific Title
Observational cohort with embedded randomised controlled feasibility trial to study pregnancy-associated progression of renal disease

Acronym
ORCHARD

Study objectives
Primary Aim:
To establish a cohort of pregnant women with CKD including longitudinal blood, urine, saliva, tongue scraping samples to enable future embedded randomised controlled trials

Secondary Aim:
To determine the relationship between maternal factors and rates of change in maternal renal function, maternal complications and neonatal adverse outcomes
Sub study (ORCHARD-BEET):
The aim of this investigation is to determine the feasibility and acceptability of recruiting pregnant women with chronic kidney disease (CKD) to a trial of an intervention to prevent progression of the disease

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 10/01/2020, West of Scotland Research Ethics Service, REC 3 (Ground Floor, Ward 11, Dykebar Hospital, Grahamston Road, Paisley PA2 7DE, UK; +44 (0)1413140211; WOSREC3@ggc.scot.nhs.uk), REC ref: 19/WS/0197 (ORCHARD Observational study)
2. Approved 13/02/2020, London City & East Research Ethics Committee (Bristol Research Ethics Committee Centre, Whitefriars, Level 3, Block B, Lewins Mead Bristol. BS1 2NT, UK; +44 (0)207 104 8171; nrescommittee.london-cityandeast@nhs.net), REC ref: 20/LO/0009 (ORCHARD BEET study)

Primary study design
Other

Study design
Trial within a cohort (embedded randomized controlled feasibility trial)

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Progression of chronic kidney disease in pregnancy

Interventions
Eligible women will be identified from GP referral letters, antenatal or outpatient clinic visits and from health professionals on antenatal wards.
During pregnancy, a blood and urine test will be done at the same time as other blood and urine tests required as part of routine antenatal care (a maximum 3 visits in pregnancy and 2 post-partum visits at 6 weeks and 6 months after delivery). There will be at least one blood and urine test in pregnancy from the time informed consent is given.
- Blood and urine samples will be taken by a research midwife/practitioner, processed immediately and then stored at -80°C for future measurements (e.g. plasma nitrate/nitrite concentrations).
Optional samples will be collected for future research projects including:
- Tongue scrapings placed into a sterile sealed container and stored at -80°C for bacterial community profiling using Next-Generation sequencing for future assessment of relationship with oral nitrate conversion to nitrite.
- Salivary samples (x2) will be collected into sterile tubes, and either processed immediately or stored at -80°C for future measurements (e.g. nitrate/nitrite concentrations and enzymatic activity assays).
If a woman delivers at another hospital the research team will attempt to get the relevant information from the maternity unit used with the permission of the woman.

Following delivery, participants will be asked if they can be contacted to give additional blood and urine samples at 6 weeks and 6 months postpartum. This visit can be coordinated with other postnatal appointments or booked separately after delivery.
If the woman is unable or unwilling to give all samples at each visit she will not be excluded from the main study.

Sub study (ORCHARD-BEET):
Women with CKD will be randomised to take dietary nitrate supplement or no treatment and kidney function at 6 months after delivery will be assessed.
Randomisation to Orchard Beet will take place once patient is recruited to the main ORCHARD study. Minimisation randomisation will immediately be performed electronically after data entry to ORCHARD observational study by the local site team with confirmation emails automatically generated to relevant individuals detailing the allocation by King's Clinical Trials Unit.
Minimisation will be used to ensure balance between the groups with respect to study centre (8 centres), highest serum creatinine concentration prior to randomisation (≤90 µmol/L, 91-120 or >120 µmol/L) and gestation at recruitment (<12 weeks, 12-15+6 weeks, 16-19+6 weeks, ≥20 weeks).

Dietary nitrate: 70 mls 'Beet It Sport shot'; http://beet-it.com/sport
Active ingredient: 400 mg nitrate/ 6.45 mmol nitrate)
Suppliers Name: James White

Intervention Type
Supplement

Primary outcome(s)
ORCHARD: Recruitment per centre per month (determined from screening /enrolment logs)

Sub-study (ORCHARD-BEET): Recruitment rate of pregnant women with CKD per site per month (determined from screening /enrolment logs)

Key secondary outcome(s)
ORCHARD study:
1. Maternal factors will be measured using demographic and clinical data obtained from medical notes, patient interview, examination and blood/urine tests at baseline
2. Maternal renal function will be measured using serum creatinine and urine protein measurement (albumin creatinine ratio, protein creatinine ratio OR 24 hour urine protein) at baseline, each trimester, 6 weeks post-partum and 6 months post-partum
3. Maternal complications will be measured using maternal outcomes (mode, timing, indications for and complications of delivery) and adverse events as defined by the protocol and identified with medical notes and patient interview at each trimester visit, 6 weeks post-partum and 6 months post-partum
4. Neonatal adverse outcomes will be measured using review of medical notes at 6 weeks post-partum to assess mode and outcome of delivery, Apgar scores, measures of size and weight, admission to Neonatal ICU or Special Care Unit
Sub study (ORCHARD-BEET):
5. Number of eligible women with CKD will be assessed from recruitment logs
6. Feasibility and acceptability of the intervention to clinicians and women (including reasons for declining, retention during study and participant attitudes) will be measured using by short semi-structured interviews of local principal investigators (face-to-face or by telephone) and acceptability of women will be assessed with "Survey Monkey" questionnaire sent 2-4 weeks

after recruitment, 32+0-35+6 weeks' gestation, 6-12 weeks after delivery asking whether they enjoyed taking their beetroot juice, whether they would be willing to take it in future pregnancies and whether they would recommend it to other pregnant women with chronic kidney disease
7. Adherence and reasons for non-adherence will be measured using daily diaries of participants which are reviewed and entered into an adherence log on the Orchard database at each trimester and 6 weeks post-partum
8. Mean and SD for primary outcome will be estimated to inform sample size for a definitive trial

Completion date
30/04/2024

Eligibility

Key inclusion criteria
ORCHARD study:
1. Pregnant women with CKD Stages 2-5 including those with renal transplants i.e. pre-pregnancy eGFR <90mls/min/1.73m2 OR pregnancy creatinine >70 µmol/l (or > 80 µmol/l if Black) with no clinical suspicion of acute kidney injury
2. <24+6 weeks' gestation
3. ≥18 years old
4. Willing and able to provide written informed consent

Sub study (ORCHARD-BEET):
5. Consented to observational ORCHARD study
6. Agreed to be contacted about future research studies

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Female

Key exclusion criteria
ORCHARD study:
1. Already established on haemodialysis or peritoneal dialysis
2. Multifetal pregnancy
3. Major life-threatening congenital abnormality

Sub study (ORCHARD-BEET):
4. Known allergy to beetroot

Date of first enrolment
01/02/2020

Date of final enrolment
30/04/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
King's College Hospital NHS Foundation Trust
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
Trust Offices, Guys Hospital
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre
Barts Health NHS Trust
The Royal London Hospital
Whitechapel
London
United Kingdom
E1 1BB

Study participating centre
Manchester University NHS Foundation Trust
Cobbett House
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Nottingham University Hospital NHS Trust
Trust Headquarters
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
University Hospitals Birmingham NHS Trust
Trust HQ, PO Box 9551
Queen Elizabeth Medical Centre
Edgbaston
Birmingham West
United Kingdom
B15 2TH

Study participating centre
Imperial College Heathcare NHS Trust
St Mary's Hospital
Praed Street
London
United Kingdom
W2 1NY

Study participating centre
University Hospitals of Leicester NHS Trust
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Sponsor information

Organisation
King’s College Hospital NHS Foundation Trust

Funder(s)

Funder type
Charity

Funder Name
Kidney Research UK

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from the Chief Investigator, Dr Kate Bramham (kate.bramham@kcl.ac.uk).
- Type of data: Fully anonymised individual patient demographic and clinical data
- Suitable for all types of analyses conditional on ethics approval and approval by the Orchard Trial Group

- Mechanism: Obtain REC approval for study, contact Dr Bramham, request considered by Orchard Trial Group and if deemed appropriate then data sharing agreement drafted and requested data transferred
- Consent: Will be sought from Orchard participants at recruitment for their data to be used in future studies subject to ethics approval

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
HRA research summary			28/06/2023	No	No
Other publications		17/05/2024	20/05/2024	Yes	No