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A study to test whether spironolactone and dietary nitrate (as beetroot juice) alter blood vessel stiffness in Type 2 diabetes

Submission date
31/01/2013

Recruitment status
No longer recruiting

Registration date
31/01/2013

Overall study status
Completed

Last Edited
11/03/2022

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Blood vessel damage in diabetes, and probably in people who are overweight, is a major threat to the health of anyone with the condition. There is strong evidence that people with diabetes develop stiffening of their arteries due to excess scar formation in blood vessel walls. We want to test whether a treatment usually given for high blood pressure and a vegetable juice can help prevent the scarring and improve blood vessel function.

Who can participate?
Men and women aged 18 to 80 years with diagnosed Type 2 diabetes, or at risk of diabetes, for example by being overweight and found to have raised blood sugar.

What does the study involve?
If you decide to take part and are suitable for the study we will ask you to come to the Clinical Research Facilities (St Thomas Hospital or Kings College Hospital) for a screening visit where we will measure your blood pressure (BP), height, weight and ask you questions about your medical history, we will then take a blood sample and a urine sample. If you are eligible, we will then use non-invasive and painless devices to measure the health of your blood vessels. The devices generally use a simple cuff (as used for blood pressure). During these, we will ask you to keep still for a few minutes while we fit and inflate cuffs around your ankles and arms. There is also a small cuff on one side of the neck which is not inflated above 60mmHg (less tight than a mans tie). They have all been found to be entirely safe. We will also measure the number of small vessels in your finger with a simple, painless microscope, which takes about 5 minutes. An Electrocardiogram (ECG) and an Echocardiogram to assess how well the heart pumps will be offered to you at the start and end of the study. These measures will be repeated up to 5 times in the study, after 2 weeks, then every 3 months from the start of the treatment for 1 year. Visits will be required after 2 weeks after starting treatment and at month 2 where we will only take a blood sample and measure your BP. If you are willing we will also ask you to collect your urine for 24h 3 to 4 times during the study and ask you to wear a cuff on your arm measuring your BP for 24h, which also measures blood vessel stiffness. At your second visit we will provide you with the treatment to take during the study. This will be pills, either as spironolactone or doxazosin

which both lower BP and a beetroot juice or a control juice (beetroot juice but without Nitrate). You take these pills and juice daily with your current treatment. These treatments are allocated by randomization, that is purely by chance as generated by computer. Neither you nor we decide which treatment you will receive; also neither you nor we will know which you are taking until the study ends, so that it will not affect the results.

What are the possible benefits and risks of participating?
You will have regular vascular and blood pressure check up that goes beyond your routine care. We will check your kidney function often and we will contact you if there are any problems. At the end of the study you will receive the results of all your tests. We will reimburse you travel expenses for a maximum of £15 per visit and some refreshment will be provided at the end of each visit. Taking blood samples may cause minor discomfort with a small chance of minor bruising. Many measures of BP can make the arm feel a bit squeezed and leave a few marks which go soon after. Vascular measures are very similar to BP. Most people have no problems with either type of pill but as always, some people have side-effects. These are not common but see list below here. For spironolactone, the blood potassium increases a little (harmless unless it goes very high, usually when kidney function is impaired, which is why we measure it at the start and through the study). Other rarer problems can include a skin rash and in men some tenderness in the nipples (very rare in women). Occasionally, problems with erectile function can occur in men but viagra-like treatment helps (this can be provided free by your GP). Doxazosin has few problems but dizziness can occur.

Where is the study run from?
St Thomas Hospital or Kings College Hospital (UK)

When is the study starting and how long is it expected to run for?
The recruitment will run from February 2013 for 2 years.

Who is funding the study?
FUKUDA Denshi Japan

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
13648

Study information

Scientific Title
A study to test whether spironolactone and dietary nitrate (as beetroot juice) (I) compared to controls, alter blood vessel function, measured as the cardiac-ankle vascular index (O) or as arterial pulse wave velocity (O) in Type 2 diabetes (P): a randomised trial

Acronym
Vasera Study

Study objectives
Blood vessel damage in diabetes is a major threat to the health of anyone so diagnosed. There is strong evidence that people with diabetes develop stiffening of their arteries due to excess collagen formation in the blood vessel walls.

Spironolactone is an antagonist of the major hormone (aldosterone) that may induce this collagen excess. Similarly there is quite good evidence that dietary Nitrate (as beetroot juice) may help protect the blood vessels.

The aim of the trial is to find out whether spironolactone and dietary nitrate can improve vascular function in a population of Type 2 diabetes patients and subjects at risk of diabetes.

The physiological measures of vascular function are the cardiac-ankle vascular Index (CAVI), Pulse Wave Analysis (PWA), Pulse Wave Velocity (PWV) and central blood pressure (BP), all measured from a BP cuff device or a tonometer. We will also be looking at capillary density measures in the fingers, 24h readings of vascular function, kidney filtrations of Sodium and Potassium and other cardiovascular related markers.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee- London Central, 21/12/2012, ref: 12/LO/1850

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Diabetes Research Network; Subtopic: Type 2; Disease: Cardiovascular disease, Hypertension, Diabetic Control, Nutrition, Pre Diabetes

Interventions
Drugs: Spironolactone at 12.5 mg titrated up to 25 mg or 50mg daily for 6 months, or up to 1 year if subject are willing.
Doxazosin at 4mg, titrated up to 8mg and 16mg for the same period.

Nutritional, 70ml high nitrate beetroot juice (nitrate content: 4,5mmols) from James White Drinks, 1 a day for 3 months, then a 70 ml juice with a nitrate content of 7.5mmols for another 3 months,up to 1 year if willing

Control: 70ml control beetroot juice from James White Drinks, 1 a day for 6 months, up to 1 year if willing

Follow Up Length: 12 month(s)

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Spironolactone, doxazosin

Primary outcome measure
Vascular function measured as CAVI (Cardio-Ankle Vascular index); Timepoint(s): baseline visit, 2 weeks, 2,3,6,12 months

Secondary outcome measures
1. Capillary density; Timepoint(s): baseline, 3 and 6 months
2. Hormones related to diabetes and hypertension; Timepoint(s): baseline, 2 weeks, 2, 3, 6, 12 months

3. PWV (Pulse Wave Velocity) in relation to changes in BP (Blood Pressure); Timepoint(s): Baseline, 2 weeks, 2, 3, 6, 12 months
4. Urinary Sodium, Potassium; Timepoint(s): baseline, 2 weeks, 2,3, 6,12 months

Overall study start date
01/02/2013

Completion date
02/06/2014

Eligibility

Key inclusion criteria
1. Anyone (male or female, age 18-80) with diagnosed type 2 Diabetes or at risk of type 2 Diabetes (being overweight BMI >= 27 kg/m2) or found to have impaired glucose tolerance by fasting glycaemia or by glucose tolerance testing will be eligible. Please see under exclusion criteria for limits to this
2. Participants need to be able to understand the protocol and be willing to comply with it

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
80 Years

Sex
Both

Target number of participants
UK Sample Size: 120

Total final enrolment
126

Key exclusion criteria
1. Ongoing (chronic) illness of any type interfering with patient ability to participate
2. Major complications restricting mobility including active foot ulceration or amputation may be exclusion criteria, but only if the patient feels they cannot manage
3. Previous adverse reactions to Spironolactone or Doxazosin. (If patients are already on either of these, we can discuss alternatives)
4. Renal function by eGFR < 45 mls per minute (approximately - i.e. if one test is around 43 and another is around 46 the average of around 45 is acceptable)
5. Objective renal function tests for creatinine > 180 umol/l (when eGFR will be < 45 mls/ min).
6. All other aspects of diabetic control will be acceptable except gross disturbances of glycaemia

with HbA1c > 11% and fasting random glucose > 12mmol/l. Those will not be indications to withdraw patients, but only as exclusions for entry (& once improved can become eligible).
7. For women: being pregnant or breastfeeding for the duration of the study

Date of first enrolment
01/02/2013

Date of final enrolment
02/06/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
King's College London
London
United Kingdom
SE1 9NH

Sponsor information

Organisation
King's College London (UK)

Sponsor details
Medicine
Franklin-Wilkins building
150 Stamford street
London
England
United Kingdom
SE1 9NH

Sponsor type
University/education

Website
http://www.kcl.ac.uk/

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Industry

Funder Name
Fukuda Denshi UK Ltd (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results	abstract	26/09/2017	04/06/2019	No	No
Results article		01/05/2020	24/06/2021	Yes	No
Results article		29/05/2021	11/03/2022	Yes	No
HRA research summary			28/06/2023	No	No